"To study the prevalence and risk factors for pulmonary hypertension and myocardial dysfunction in post pulmonary tuberculosis patients of age group 1-18 years."

Thesis submitted to the faculty of

ALL INDIA INSTITUTE OF MEDICAL SCIENCES BHOPAL

For the award of the degree MD in the subject of

PEDIATRICS

By

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CERTIFICATE

This is to certify the thesis entitles "To study the prevalence and risk factors for pulmonary hypertension and myocardial dysfunction in post pulmonary tuberculosis patients of age group 1-18 years." is bonafide and genuine research carried out by DrShubham, under the guidance and direct supervision for the award of MD.

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DECLARATION

I, **Dr Shubham,** hereby declare that the thesis entitled "To study the prevalence and risk factors for pulmonary hypertension and myocardial dysfunction in post pulmonary tuberculosis patients of age group 1-18 years." is a bonafide and original work carried out by me under the supervision and guidance of **Dr Amber Kumar**(Associate Professor, Department of Pediatrics). The thesis or any part thereof has not formed the basis of any degree/fellowship or similar title to any candidate of any university to the best of my knowledge.

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AIIMS, Bhopal Institutional Human Ethics Committee- Student Research (IHEC-SR) in its 7th meeting held on 22nd February 2023 discussed your proposal titled **"To study the prevalence and risk factors for pulmonary hypertension and myocardial dysfunction in post pulmonary tuberculosis patient of age group 1-18 years"** and evaluated it for suitability for your dissertation as required for fulfilment of MD/MS program.

Following members attended the meeting:

1. Prof. D. K. Pal, Former HoD Community Medicine, GMC, Bhopal.....Chairperson
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The decision of the committee is as follows:

The AIIMS, Bhopal IHEC-SR approves your research protocol. All research related activities must begin only after the date of this approval. The validity of this approval is till two years from the date of issuance. Please submit a closure report / renewal request before expiration of the validity for this approval.

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LIST OF ABBREVIATIONS:

TB	Tuberculosis
WHO	World Health Organisation
NTEP	National Tuberculosis Elimination Programme
PTB	Pulmonary tuberculosis
EPTB	Extra Pulmonary Tuberculosis
ATT	Anti tubercular treatment
COPD	Chronic Obstructive Pulmonary Disease.
PH/Pulmonary HTN	Pulmonary Hypertension
PAH	Pulmonary Arterial Hypertension
IPAH	Idiopathic Pulmonary Arterial Hypertension
PAH-CHD	Pulmonary Arterial Hypertension – Congenital Heart Disease
PPHN	Persistent Pulmonary Hypertension of Newborn
HPAH	Hereditary Pulmonary Arterial Hypertension
RHC	Right Heart Catheterisation
WSPH	World Symposium on Pulmonary Hypertension
Mpap/MPAP	mean Pulmonary Arterial Pressure
PVR	Pulmonary Vascular Resistance
PVR	Pulmonary Vascular Resistance index
WU	Woods Unit
PVD	Pulmonary Vascular Disease
CO	Cardiac Output
PAWP	Pulmonary Arterial Wedge Pressure
IpcPH	Isolated precapillary pulmonary hypertension

CpcPH	Combined pre and post pulmonary hypertension
HIV	Human immunodeficiency virus
PVOD	Pulmonary venous occlusive disease
RV	Right ventricle
ECG	Electrocardiography
sPAP	Systolic pulmonary arterial pressure
TRV	Tricuspid regurgitation Velocity
TRPG	Tricuspid regurgitation pressure gradient
CT	Computed tomography
RV/LV	Right ventricle/left ventricle
USG	Ultrasonography
MRI	Magnetic resonance imaging
TDL	Tuberculosis destroyed lung
PTLD	Post tuberculosis destroyed lung
MMP	Matrix metalloproteinases
FEV1	Forced expiratory volume (1^{st} sec)
FVC	Functional Vital capacity
FEF	Forced expiratory flow
CXR	Chest xray
CTD	Connective tissue disease
WHO-FC	World healt organisation functional classification
PHVD	Pulmonary hypertension vascular disease
NT-proBNP	N terminal pro brain natriureteric peptide
CI	Cardiac index

LMIC	Low and middle income countries
OR	Odd's ratio
ECHO	Echocardiography
IVS	Interventricular septum
RVSP	Right ventricle systolic pressure
PASP/sPAP	Pulmonary artery systolic pressure/Systolic pulmonary artery pressure
OPD	Outpatient department
TDI	Tissue doppler imaging
TR/PR	Tricuspid regurgitation/pulmonary regurgitaion
CW DOPPLER	Colour wave doppler
PAAT/PVAT	Pulmonary artery acceleration time /Pulmonary velocity acceleration time
MPI	Myocardial performance index
PADP	Pulmonary artery diastolic pressure
RVED/RVEDP	Right ventricle end diastolic pressure
SD	Standard deviation
AFB	Acid Fast Bacilli
CBNAAT	Cartridge Based Nucleic Acid Amplification Test

INTRODUCTION

Tuberculosis (TB) is a communicable disease that can affect people from any age group. It is caused by gram positive acid fast bacilli Mycobacterium tuberculosis which is an obligate aerobe. It can affect any part of body but is mainly an infection of lung. Disease is spread when people who are sick with TB expel bacteria in the air. Clinical manifestations can be in form of primary pulmonary disease, progressive primary pulmonary disease, pleural effusion, pericardial disease, disseminated lymphohematogenous disease. It can affect lymph nodes, central nervous system, skin and soft tissue, joint and musculoskeletal system, gastrointestinal and genitourinary system. WHO Global TB Report 2022 states that 21.4 Lakh TB cases notified in India in 2021, 18% higher than 2020(1). Over 22 crore people screened for TB in 2021 across the country for early detection and treatment of TB .The prevalence of childhood tuberculosis (TB) is alarming. 3.42 lakh children (0–14 years old) in India are predicted to contract TB each year, making up nearly 6% of all TB cases reported to NTEP in 2020(1,2). One lakh children with TB (0 to 14 years old) were reported to the NTEP in 2020, and an additional 1.4 lakh children (15 to 18 years old) were reported to the NTEP(3). Children make up 6-7% of all patients treated annually under the NTEP, on average. Nearly one third of the children with TB worldwide are from India. In our nation, children under the age of 14 make up 35% of the population and are thought to be responsible for 10% of the caseload(4).

Although extra-pulmonary TB (EPTB) affects children more frequently than adults, pulmonary TB is the most prevalent type of TB in kids. Post tuberculosis sequelae, most often occurring in the lungs following the destruction of lung tissue caused by Mycobacterium tuberculosis, include diseases such as chronic obstructive lung

disease(COPD), pulmonary hypertension(PH), bronchiectasis, and secondary non-tuberculosis infections, all of which require appropriate screening and diagnosis to guide subsequent therapies. As a result of the parenchymal destruction of the lung tissue brought on by pulmonary tuberculosis, which can also affect the vascular system and cause endarteritis and vasculitis, there may be a reduction in the cross-sectional area of the pulmonary vasculature and consequently cause pulmonary hypertension(5). Patients with pulmonary hypertension typically present with desaturation with even light exercise, dyspnea that is out of proportion to their radiological profile, and occasionally overt heart failure with pedal edema, elevated jugular venous pressure, and painful hepatomegaly. Due to numerous diagnostic difficulties, pulmonary hypertension continues to be an understudied post-tuberculosis lung sequela. This process requires specialised tools, as well as skilled personnel for administering medications and monitoring hemodynamics—both of which are not easily accessible in settings with few resources(6).

REVIEW OF LITERATURE

1.PULMONARY HYPERTENSION

2.POST PULMONARY TB PULMONARY HYPERTENSION

1.PULMONARY HYPERTENSION

Pulmonary hypertension (PH) is a pathological condition which can have several clinical manifestations and be linked to a number of respiratory and cardiovascular disorders(7). While paediatric pulmonary arterial hypertension (PAH) is linked to several extra diseases and difficulties, it shares many characteristics with adult condition(8). Children's pulmonary hypertension (PH) is linked to a number of disorders that can manifest at any age. Compared to adult PH, the distribution of aetiologies in pediatric PH is very diverse with prevalence of idiopathic pulmonary arterial hypertension (IPAH), pulmonary arterial hypertension (PAH) associated with congenital heart disease (PAH-CHD), and developmental lung diseases more among children(8).

1.1Epidemiology

Pulmonary hypertension poses a significant worldwide health concern, impacting individuals of all ages. Current approximations indicate that around 1% of the global population is affected by PH. The prevalence of PH is higher in individuals over the age of 65 due to the presence of cardiac and pulmonary causes. Left heart disease is the primary cause of PH on a global scale. The second most common cause of PH is lung disease, particularly chronic obstructive pulmonary disease (COPD)(9).The annual incident rate for pediatric PH is 64 per million children . PH's etiologies in childhood differ from those in adulthood . In children,

pulmonary arterial hypertension is the most common type of PH, with the majority (82%) of cases occurring in infants with transient PAH (i.e. Persistent pulmonary hypertension of newborn PPHN or repairable cardiac shunt defects)(10). Among the children who still have PAH, the majority are diagnosed with either IPAH, HPAH, or non-reversible CHD-associated PAH. The documented rates for IPAH/HPAH and non-transient CHD-associated PAH are 0.7 and 2.2 per million children, while the prevalence is 4.4 and 15.6 per million children, respectively.(10)

1.2Definition

The definitions of PH are based on evaluating the hemodynamics through right heart catheterization (RHC). Ever since the first World Symposium on Pulmonary Hypertension (WSPH) in 1973, there has been an arbitrary definition of pulmonary hypertension (PH) as a mean pulmonary arterial pressure (mPAP) of 25 mmHg or higher at rest, which is measured through right heart catheterization at rest in supine position.(11) The definition of pulmonary hypertension (PH) in children has historically mirrored that in adults, which is a mean pulmonary arterial pressure (mPAP) of equal to or greater than 25 mmHg. In normal fetal circulation, the pulmonary arterial pressure is comparable to systemic pressure and decreases rapidly after birth, reaching levels similar to those in adults by 2–3 months of age. Due to the varying pulmonary hemodynamics during the post-natal transition, pediatric PH has been characterized as mPAP of equal to or greater than 25 mmHg after 3 months of age.(12) The 6th World Symposium on Pulmonary Hypertension suggested changing the definition of pulmonary hypertension in adults to mPAP >20 mmHg and adding PVR ⩾3WU to diagnose pre-capillary PH. However, simply having a higher than normal mean pulmonary artery pressure (mPAP) is not enough to diagnose pulmonary vascular disease (PVD) because it

could be caused by an increase in cardiac output (CO) or pulmonary artery wedge pressure (PAWP)(11).Therefore Including PVR and pulmonary arterial wedge pressure (PAWP) in the definition of pre-capillary PH is crucial to differentiate between elevated PAP caused by pulmonary vascular disease (PVD) and that caused by left heart disease , elevated pulmonary blood flow, or increased intrathoracic pressure(7).

Table 1:Haemodynamic definitions of pulmonary hypertension

Definition	Haemodynamic characteristics
PH	mPAP >20 mmHg
Pre-capillary PH	mPAP >20 mmHg PAWP ⩽15mmHg PVR >2 WU
IpcPH	mPAP >20 mmHg PAWP >15 mmHg PVR ⩽2WU
CpcPH	mPAP >20 mmHg PAWP >15 mmHg PVR >2 WU
Exercise PH	mPAP/CO slope between rest and exercise >3 mmHg/L/min
IpcPH-Isolated pre capillary pulmonary hypertension CpcPH-Combined pre and post capillary pulmonary hypertension	
mPAP-mean pulmonary artery pressure PAWP-pulmonary artery wedge pressure PVR-pulmonary vascular resistance	

Table 2: Clinical classification of pulmonary hypertension

- GROUP 1 Pulmonary arterial hypertension (PAH)
    - Idiopathic
        - Non-responders at vasoreactivity testing
        - Acute responders at vasoreactivity testing
    - Heritable
    - Associated with drugs and toxins
    - Associated with:
        - Connective tissue disease
        - HIV infection
        - Portal hypertension
        - Congenital heart disease
        - Schistosomiasis
    - PAH with features of venous/capillary (PVOD/PCH) involvement
    - Persistent PH of the newborn
- GROUP 2 PH associated with left heart disease
    - 2.1 Heart failure:
    - 2.1.1 with preserved ejection fraction
    - 2.1.2 with reduced or mildly reduced ejection fraction
    - 2.2 Valvular heart disease
    - 2.3 Congenital/acquired cardiovascular conditions leading to post-capillary PH
- GROUP 3 PH associated with lung diseases and/or hypoxia
    - 3.1 Obstructive lung disease or emphysema

○ 3.2 Restrictive lung disease ○ 3.3 Lung disease with mixed restrictive/obstructive pattern ○ 3.4 Hypoventilation syndromes ○ 3.5 Hypoxia without lung disease (e.g. high altitude) ○ 3.6 Developmental lung disorders
• GROUP 4 PH associated with pulmonary artery obstructions ○ 4.1 Chronic thrombo-embolic PH ○ 4.2 Other pulmonary artery obstructions
• GROUP 5 PH with unclear and/or multifactorial mechanisms ○ 5.1 Haematological disordersd ○ 5.2 Systemic disorders ○ 5.3 Metabolic disorders ○ 5.4 Chronic renal failure with or without haemodialysis ○ 5.5 Pulmonary tumour thrombotic microangiopathy ○ 5.6 Fibrosing mediastinitis

1.3Diagnosis

1.3.1 Clinical features

The primary symptoms of pulmonary hypertension (PH) are connected to the dysfunction of the right ventricle (RV) and are usually seen during physical activity in the initial stages of the condition (13). The most prominent symptom is difficulty breathing during increasingly minimal physical effort. Additional common symptoms and signs are correlated with the phases and seriousness of the illness and includes fatigue palpitations,hemoptysis,wheezing ,cough,lower respiratory tract infections .

1.3.2 Electrocardiogram

Typical ECG abnormalities in PH

• P pulmonale (P>0.25 mV in lead II)

• Right or sagittal axis deviation (QRS axis >90° or indeterminable)

• RV hypertrophy (R/S >1, with R >0.5 mV in V1; R in V1 + S in lead V5 >1 mV)

• Right bundle branch block—complete or incomplete (qR or rSR patterns in V1)

• RV strain pattern (ST depression/T-wave inversion in the right precordial V1–4 and inferior II, III, aVF leads)

• Prolonged QTc interval

1.3.3 Chest Xray

- In the PA View, there are dilated main pulmonary arteries (PAs) on the right, left, or both sides.

- Right ventricular enlargement causes fullness of the retro-sternal space.
- There is gross dilatation of the pulmonary bay, leading to fullness.

1.3.4 Echocardiography

PH results in RV pressure overload and dysfunction, which echocardiography can detect. Due to the diverse nature of pulmonary hypertension (PH) and the unique shape of the right ventricle (RV), there is no single echocardiographic measure that consistently indicates the status of PH and its underlying cause. As a result, a thorough echocardiographic assessment for suspected PH involves determining the systolic pulmonary arterial pressure (sPAP) and identifying additional indicators that suggest PH, with the goal of establishing an echocardiographic probability level for PH(7). The estimation of sPAP relies on the highest tricuspid regurgitation velocity (TRV) and the tricuspid regurgitation pressure gradient (TRPG) derived from TRV, while excluding pulmonary stenosis. This estimation also considers non-invasive assessments of RA pressure. A peak TRV greater than 2.8 m/s could indicate pulmonary hypertension (PH); however, TRV alone cannot reliably determine the presence or absence of PH(14)

1.3.5 CT Chest

The CT findings that indicate the existence of pulmonary hypertension (PH) consist of an increased pulmonary artery (PA) diameter, a PA-to-aorta ratio greater than 0.9, and enlargement of the right heart chambers. A set of three criteria (PA diameter ≥30 mm, RVOT wall thickness ≥6 mm, and septal deviation ≥140° [or RV:LV ratio ≥1]) is extremely indicative of PH.(15)

1.3.6 Abdominal USG

It is important to include an abdominal ultrasound as part of the thorough diagnostic evaluation for patients who have recently been diagnosed with PH, especially if there are concerns about liver disease. The primary goal is to look for signs of liver disease, portal hypertension, or portocaval shunt (Abernethy malformation).(7)

1.3.7 MRI

The measurement of blood flow in the pulmonary artery, aorta, and vena cava can be achieved using cMRI, enabling the quantification of stroke volume (SV), intracardiac shunt, and retrograde flow. A comprehensive view of the heart and pulmonary vasculature can be obtained by integrating contrast MR angiography, pulmonary perfusion imaging, and late gadolinium-enhancement imaging of the myocardium.(7)

1.3.8 Right heart catheterization

Right heart catheterization is the gold standard for diagnosing and classifying PH. Being an invasive procedure not routinely practised in paediatric population.

1.4 Pathophysiology of development of pulmonary hypertension:

The interaction between various cell types in the lung, such as vascular cells, immune cells, and circulating cells, propels the biological processes**.** The main cells responsible for the development of the condition are pulmonary artery endothelial cells, pulmonary artery smooth muscle cells, and pulmonary artery fibroblasts. Dysfunction of pulmonary artery endothelial cells can be attributed to various factors, including shear stress, direct vascular injury, and inherent abnormalities.(16)

The impairment of endothelial function leads to reduced generation of vasodilators such as nitric oxide and prostacyclin, as well as heightened production of procontractile agents like endothelin 1.(17)

A. Dysfunctional angiogenesis:

Dysfunctional angiogenesis plays a significant role in the development of pulmonary arterial hypertension. The lining of blood vessels in the lungs consists of a monolayer of pulmonary artery endothelial cells, which is crucial for maintaining vascular balance. Changes in these endothelial cells, induced by factors such as shear stress, toxins, or genetic abnormalities, can result in dysfunctional angiogenesis.(18) In the early stages of vascular injury, pulmonary artery endothelial cells become proapoptotic, leading to the loss of pulmonary microvessels. Among the cells that survive the initial insult, it is hypothesized that an apoptosis-resistant phenotype emerges, which is associated with a hyperproliferative state contributing to the formation of plexiform lesions and the obliteration of lung vessels. Ultimately, in the terminal stages of pulmonary arterial hypertension, pulmonary artery endothelial cells may transition to a senescent phenotype, resulting in the disease becoming irreversible.(19)

B. Inflammation and immune dysregulation:

Interleukin 6 and interleukin 1β play significant roles as proinflammatory cytokines in pulmonary arterial hypertension, directly influencing the proliferation, migration, and differentiation of pulmonary artery endothelial cells, pulmonary artery smooth muscle cells, and immune cells.(20) Autoantibodies and localized lymph follicles have been linked to the promotion of inflammation and immune activation in pulmonary arterial hypertension.

C. Genetics in pulmonary arterial hypertension:

Several mutations that likely have a causal role in pulmonary arterial hypertension, such as BMPR2, EIF2AK4, TBX4, ATP13A3, GDF2, SOX17, AQP1, ACVRL1, SMAD9, ENG, KCNK3, and CAV1, have been identified through patient cohort surveys . (21)BMPR2 mutations are the most frequently occurring and extensively studied. They have been found in 70-80% of patients with heritable pulmonary arterial hypertension and in 10-20% with idiopathic pulmonary arterial hypertension. These mutations are associated with increased susceptibility, earlier disease onset, and heightened severity and mortality of the disease.(22)

D. Metabolic Alteration:

In pulmonary arterial hypertension, there is a shift from oxidative phosphorylation to glycolysis, which is known as the Warburg effect. Altered metabolism in pulmonary arterial hypertension is characterized by increased cytoplasmic glycolysis and glutaminolysis, along with impairments in mitochondrial biogenesis and fatty acid oxidation(23). Additionally, reduced mitochondrial metabolism is observed in pulmonary arterial hypertension. Mitochondrial abundance is lower in pulmonary artery endothelial cells and pulmonary artery smooth muscle cells, and decreased oxygen consumption and mitochondrial DNA are

present in pulmonary artery endothelial cells. Patients with pulmonary arterial hypertension exhibit increased pyruvate dehydrogenase inhibitory kinase activity in the pulmonary arteries, leading to uncoupled glycolysis and reduced mitochondrial pyruvate utilization. (24)

E. Sex hormone signalling:

Females have a higher prevalence of pulmonary arterial hypertension, with a female to male ratio in all forms of pulmonary arterial hypertension of 1.4-4.1 to 1. Most studies have concentrated on the impact of 17β-oestradiol in pulmonary arterial hypertension, but other sex hormones have also been reported to have effects. Some studies have connected oestrogens and their metabolites to the onset of pulmonary arterial hypertension, and increased levels of estrogen (from medication or due to pregnancy) have been linked to pulmonary arterial hypertension.(25)

F. Right ventricle dysfunction:

The alterations in inflammatory mediators, the influx of neutrophils and macrophages, dysfunction of small blood vessels, cell death, heightened oxidative stress, changes in metabolism, development of fibrosis, and modifications in mechanical properties all contribute to the progression of right ventricular failure(26). Initially, the right ventricular adaptation to pulmonary arterial hypertension or pulmonary hypertension is characterized by compensatory hypertrophy and a 4- to 5-fold increase in contractility in response to the increased workload.(27)

1.5 TREATMENT OPTIONS

Table3: Management strategies for pulmonary hypertension

<table>
<tr><td colspan="3">MANAGEMENT STRATEGIES</td></tr>
<tr><td colspan="2">A. Medical management</td><td rowspan="4">B. Interventional therapy
• Baloon atrial septostomy
• Pott’s procedure
• Pulmonary artery denervation</td></tr>
<tr><td>Calcium channel blocker</td><td>Amlodipine, diltiazem, nifedipine</td></tr>
<tr><td>Endothelin receptor antagonists</td><td>Ambrisentan
Bosentan,
Macitentan</td></tr>
<tr><td>Phosphodiesterase 5 inhibitors</td><td>Sildenafil
Tadalafil</td></tr>
<tr><td>Prostacyclin analogues</td><td></td><td rowspan="5">C. Lung Transplantation</td></tr>
<tr><td>Prostacyclin receptor agonist</td><td>Beraprost
Treprostanil</td></tr>
<tr><td>Prostacyclin receptor agonist</td><td>Selexipeg</td></tr>
<tr><td>Soluble guanylate cyclase stimulator</td><td>Riociguat</td></tr>
<tr><td></td><td></td></tr>
</table>

2.POST TB sequelae and lung health:

After recovering from tuberculosis, patients may experience a variety of outcomes, ranging from having no symptoms at all to experiencing significant disability. Extensive structural damage of the lung caused by Mycobacterium tuberculosis infection is known as tuberculosis destroyed lung (TDL). Widespread bronchial distortion, bronchiectasis, pulmonary fibrosis, cavitation, caseous necrosis, lymph node necrosis, and lymphatic obstruction are the manifestations of this damage, leading to the loss of normal lung function.(28)

PTLD encompasses a range of disorders that impact both large and small air passages (bronchiectasis and obstructive lung disease), lung tissue, pulmonary blood vessels, and pleura, and can be further complicated by co-infection and bleeding from the lungs. Factors that increase the risk of PTLD include experiencing multiple episodes of tuberculosis, tuberculosis that is resistant to drugs, delays in diagnosis, and potentially smoking.(29)

PTLD arises from the interaction between the direct harm caused by the tuberculosis bacteria in the lower respiratory system and the body's immune response . These mechanisms cause airway deformation, decreased flexibility, breakdown of the muscular elements of bronchial walls, or harm to the lung tissue and blood vessels, resulting in structural abnormalities and anatomical distortion in imaging, as well as abnormal respiratory function with irregular spirometry, modified lung capacities, and reduced diffusing capacity.(30)

The exact processes involved are not completely known, but there are four crucial elements:

(1) the creation and resolution of granulomas,

(2) the production of cytokines like tumor necrosis factor alpha and interleukins,

(3) transcription factors such as hypoxia-inducible factor, and

(4) enzymes like matrix metalloproteinases (MMP).(31)

Table 4: Clinical patterns of PTLD

Compartment	Clinical Pattern	Definition
Airways	TB associated obstructive lung disease	Airway obstruction (FEV1/FVC ratio<0.7)
	Bronchiectasis	CT definition – evidence of airway dilatation > diameter of adjacent vessel, or non-tapering, or CXR definition – evidence of ring shadows and tramlines
Parenchyma	Cavitation	A gas-filled space either within an area of pulmonary consolidation or surrounded by a thin wall
	Parenchymal destruction	Extensive destruction of lung tissue, with a gas-filled space/collapsed parenchyma occupying the volume of ≥1 lobe
	Fibrotic change	Areas of parenchymal scarring with associated volume loss

	Aspergillus-related lung disease	Evidence of aspergilloma on imaging or chronic pulmonary aspergillosis on imaging and blood testing
Pleural	Chronic pleural disease	Evidence of pleural thickening on CXR or CT imaging
Pulmonary vascular	Pulmonary hypertension	Elevated pulmonary artery pressures, as estimated using Doppler echocardiography or measured at right heart catheterisation

2.1Epidemiology of post TB pulmonary hypertension:

The risk of developing pulmonary hypertension (PH) can be affected by tuberculosis (TB) at different stages, from the initial active infection to the post-TB period. Studies on active TB have long reported the occurrence of PH, with current prevalence ranging from 8% to 27%.(32)

After completing treatment for the initial TB episode and resolution of TB symptoms, PH may be identified approximately 5–11 years later. The disparity in timing may be due to different subtypes or pathogenic pathways of post-TB PH. Some cases may stem from active pulmonary TB and either resolve or persist, while others may be purely related to post-TB occurrences, manifesting years after the initial TB episode.(33)

Table 5 :Factors affecting development of post-TB pulmonary hypertension:

TB and PTLD related	Host related	Environment related
TB related -Number of episodes, -Interrupted/incomplete treatment -Drug-resistant TB -VTE event during active TB	Age 40−60 years Male sex HIV infection CTD Diabetes mellitus	Smoking Biomass exposure Occupational exposure Socioeconomic circumstances Illicit drugs Medication
Post-TB lung disease (PTLD) -Parenchymal damage -Pulmonary functional abnormalities		

2.2 Mechanism of development of pulmonary hypertension:

The pathophysiological mechanisms that underlie the development of pulmonary hypertension in patients with pulmonary tuberculosis are still not fully understood.

The connection between tuberculosis and pulmonary hypertension is intricate, with multiple factors that contribute to a higher risk of PH in individuals who have had tuberculosis. Post-tuberculosis pulmonary hypertension (post-TB PH) arises from a combination of factors.

Pulmonary tuberculosis may result in lung damage by causing tissue scarring, fibrosis, and distortion of the airways and pulmonary blood vessels.The scarring can raise pulmonary vascular resistance, leading to higher pulmonary arterial pressure.

Patients who have had TB may encounter long-term hypoxia because of reduced lung capacity, which can worsen pulmonary hypertension. (34)

Recent research has shown that persistent hypercapnia, caused by the direct impact of carbon dioxide on the muscular pulmonary arteries, could also play a role in PH by leading to repeated constriction and restructuring of the pulmonary vessels. Hypercapnia is a significant contributing factor in the onset of PH.(35)

The persistent inflammation from active TB can also harm the pulmonary arteries, leading to endothelial dysfunction and higher resistance in the pulmonary circulation. This sequence of events can cause vascular restructuring, ultimately leading to pulmonary hypertension.

In cases of long-term tuberculosis, extensive damage to the lung tissue leads to the destruction of blood vessels, causing vasculitis and endarteritis. This results in a decreased cross-sectional area of the pulmonary vasculature and the development of pulmonary arterial hypertension (PAH).(36)

In addition to obstructive and restrictive abnormalities, hemoptysis, aspergilloma, bronchiectasis, fibrothorax, pleural thickening, and TB empyema are recognized as complications in individuals treated for PTB. Extensive and bilateral tuberculosis (TB) can result in pulmonary arterial hypertension (PAH) as a consequence of extensive fibrosis, leading to parenchymal distortion. The increase in pulmonary vascular resistance is thought to be the fundamental underlying mechanism that causes pulmonary hypertension (PAH).

The destruction of alveolar and capillary beds, resulting in gas exchange abnormalities and persistent hypoxia, both due to residual structural damage in the lungs, are the two primary pathological factors responsible for the development of PAH in treated PTB patients.(37)

The development of post-TB PH likely involves multiple mechanisms, broadly described as vascular bed involvement, thrombosis, arteriopathy, compressive disease, and coexisting left heart disease.(33)

Table 6: Proposed mechanisms of post-TB pulmonary hypertension:

Group1 PH	Group 2 PH	Group 3 PH	Group 4 PH	Group 5 PH
Pulmonary Arteriopathy	Left heart disease Coronary vascular and Pericardial disease	Loss of vascular bed Parenchymal fibrosis Obliterative bronchiolitis	Thrombosis Thromboembolism Microthrombi In situ thrombosis	Compressive disease Mediastinal fibrosis Lymphnode hyperplasia
Endothelial dysfunction Intimal thickening Muscular hyperplasia Vasculitis				
Vasoconstrictor/Vasodilator Endothelin/NO/Prostacyclin				
Mutations-BMPR				
Mitochondrial abnormalities				

The development of post-TB PH can have multiple causes and falls into the category of Group 5 PH. However, since most cases likely involve parenchymal damage (chronic lung disease) as the primary disease mechanism similar to other Group 3 PH causes it is classified under group 3.(33)

2.3 Severity and risk assessment :

During the physical examination, it is important to evaluate heart rate, rhythm, blood pressure, cyanosis, enlarged jugular veins, edema, ascites, and pleural effusions. The WHO-FC serves as a strong predictor of survival both at diagnosis and during follow-up. Worsening WHO-FC indicates disease progression and should prompt further investigations to identify the causes of clinical deterioration.(7)

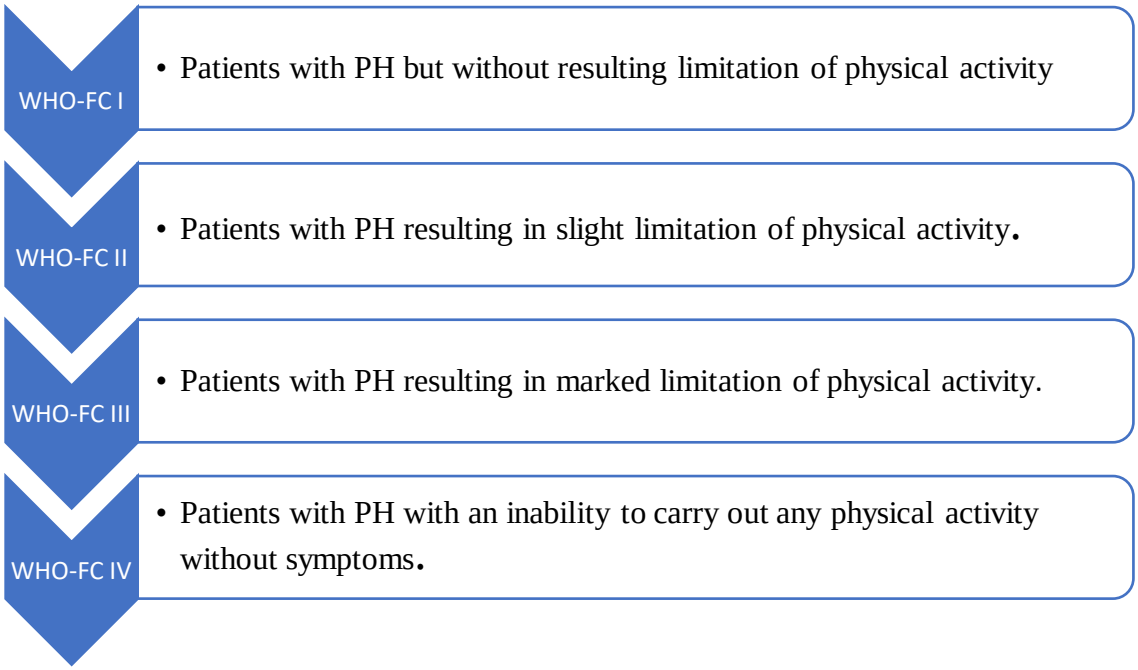

WHO-FC I
• Patients with PH but without resulting limitation of physical activity
WHO-FC II
• Patients with PH resulting in slight limitation of physical activity.
WHO-FC III
• Patients with PH resulting in marked limitation of physical activity.
WHO-FC IV
• Patients with PH with an inability to carry out any physical activity without symptoms.

Figure 1: WHO functional classification

Table 7:Determinants of risk in pediatric PH and suspected PHVD:(38)

RISK determinants	Lower risk	Higher risk
Clinical evidence of RV Symptoms	No	Yes
Progression of symptoms	No	Yes
Syncope	No	Yes
Growth	Normal	Failure to thrive
WHO functional class	I,II	III,IV
Serum NT-proBNP	Minimally or not elevated for age	Greatly elevated for age
Echocardiography	Minimal RA/RV enlargement No RV systolic dysfunction	Severe RA/RV enlargement RV systolic dysfunction
Invasive hemodynamics	CI >3.0 l/min/m2 mRAP <10 mm Hg mPAP/mSAP <0.5 Acute vasoreactivity	CI <2.5l/min/m2 mRAP >15 mm Hg mPAP/mSAP >0.75 PVRi >15 WU · m2

2.4 Prevalence of pulmonary hypertension in post tb patients:

Tuberculosis (TB) is a significant contributor to the overall disease burden worldwide. In 2021, around 10.6 million new TB cases were reported, and TB continues to be one of the primary causes of death from a single infectious agent globally(1).Low and middle income countries(LMICs) bear a disproportionate burden of TB, with over 90% of new TB cases occurring in these countries and the majority of the approximately 155 million global TB survivors residing there(39). Pulmonary TB, whether active or previously treated, often leads to permanent lung damage. Pulmonary vascular disease, a significant complication associated with TB, is probably not recognized enough.(40) The prevalence of TB-related pulmonary hypertension worldwide has not been measured before and requires assessment to understand the impact of this condition. Since TB-related pulmonary hypertension can affect young, economically active individuals and is often associated with a poor prognosis, its impact on communities is likely significant.(41,42). In countries with a high burden of TB, post-TB lung disease (PTLD) has been identified as a prevalent cause of group III PH (PH associated with lung diseases and/or hypoxia). When researchers studied groups of patients with PH from African countries, they found that 23% of patients had a history of previous or current TB.(43).After recovering from tuberculosis, lung tissue damage can result in conditions like chronic obstructive lung disease, pulmonary hypertension, bronchiectasis, and secondary non-tuberculosis infections. Proper screening and diagnosis are necessary to determine the most suitable treatments for these conditions.(44)

In a study conducted by Bhattacharyya, et al.(45) A group of 40 individuals (21 smokers and 19 non smokers) were diagnosed with pulmonary hypertension and had a history of pulmonary tuberculosis. Both groups showed similar radiological findings, including the

level of fibrosis. The age range was lower in the nonsmoker group compared to the smokers. The chronic obstructive pulmonary disease (COPD) assessment test score was worse in the nonsmoker group, and they had higher pulmonary artery (PA) pressure compared to the smokers. The spirometric pictures favored obstruction without reversibility as in COPD for the smoker group. However, those with no history of smoking had restrictive changes as in diffuse parenchymal lung disease (DPLD) in their spirometry. The smoker group had more obvious involvement of the small airways in terms of change in FEF 25-75 compared to nonsmokers.

A cross-sectional study carried out by Rajeev et al.(46) assessed 46 patients with sequelae. Among the patients, 21 (45.65%) were found to have pulmonary hypertension, and out of those, 15 (71.43%) also had cor pulmonale. The most common lesion observed was fibrosis (82.2%). Patients with combined sequelae lesions were at a higher risk compared to those with a single lesion (p=0.026; OR:4). Additionally, 61.9% of the patients exhibited a mixed pattern in spirometry, which posed a significant risk compared to patients with either one pattern. In conclusion, pulmonary hypertension is a significant complication in post-pulmonary tuberculosis sequelae. Higher risk factors included undernourishment, defaulting on treatment, and extensive lesions.(46)

An observational study (41)involving 728 patients. Among the participants, 554 (76%) were newly diagnosed with Pulmonary TB, and 174 (24%) had a previous history of Pulmonary TB. The study found that out of the 728 pulmonary TB patients, 104 (14%) were diagnosed with Pulmonary Hypertension. Among the patients with Pulmonary TB and Pulmonary Hypertension, 19 (22%) out of 86 died, compared to 51 (9%) out of 553 patients with pulmonary TB alone. The prognosis was unfavorable for those who developed Pulmonary

Hypertension as a result of Pulmonary TB. Additionally, among the 67 patients diagnosed with both Pulmonary TB and PH at the start of treatment, Doppler Echocardiography at the end of treatment revealed an increase in PA systolic pressure compared to the beginning of treatment, indicating a progression in the severity of Pulmonary Hypertension.

Rohit Chordia et al.(47), In post pulmonary tuberculosis sequelae, pulmonary hypertension is a major complication. For patients who have completed anti-tuberculosis treatment (ATT) and are experiencing symptoms of right-sided failure, early diagnosis and treatment initiation can be facilitated by echocardiography.

It's important to broaden our focus beyond managing current cases of pulmonary tuberculosis and consider the pulmonary impairment that can occur after tuberculosis, requiring a fresh perspective on post-tubercular lungs. Patients in this category should receive timely and thorough screening, diagnosis, and accurate identification of the type of pulmonary impairment (obstructive, restrictive, or mixed) to ensure appropriate guidance for comprehensive patient management and ultimately enhance their quality of life.(48)

In study by Chatterjee et al, 60 patients with pulmonary tuberculosis and lung fibrosis were included, with 41 being male (68.33% of the study population) and 19 being female (31.67%). Among the 60 patients with confirmed lung fibrosis through radiological examinations, 8 were diagnosed with pulmonary arterial hypertension (PAH)(49), making up 13.33% of the study population. Out of these eight PAH cases, three were classified as mild, four as moderate, and one as severe based on 2D echocardiography findings.

One study(50) involved 20 participants with a history of TB treatment and no other risk factors for PH. They underwent ECG, chest X-rays, lung function tests, and ECHO. After

approximately 30 months post-TB diagnosis, none of the participants showed ECHO findings indicative of PH (PAP ≥40 mmHg). However, a negative correlation was observed between the duration since diagnosis and right ventricular dysfunction as measured by tricuspid annular plane systolic excursion.

Prabhakar et al(51). out of 122 individuals aged 21 years and older with a history of pulmonary TB, 60.66% were found to have pulmonary hypertension, and among those with pulmonary hypertension, 60% had corpulmonale. The most common pulmonary TB sequelae were fibrosis, observed in 55.73% of patients, followed by bronchiectasis at 18.85%. The prevalence of mild pulmonary hypertension was 29.50%, moderate was 22.95%, severe was 8.19%, and normal was 39.34%. Corpulmonale was present in 49 cases (66%). Among patients with pulmonary hypertension, 20.27% had normal spirometry results, 12.16% had obstruction, 43.24% had probable restriction, and 24.32% had obstruction with decreased FVC.

In a study of 108 participants , average age of the participants was 52.1 years. Among the study group, 58 participants (53.7%) were females. Pulmonary hypertension was present in 48 patients (44.4%). Among all the patients, 5 (4.6%) had mild pulmonary hypertension, 15 (13.9%) had moderate pulmonary hypertension, and 28 (25.9%) had severe pulmonary hypertension. When considering age in relation to pulmonary hypertension, it was found that 3 (2.8%) patients were in the 16-40 age group, 20 (18.5%) patients were in the 41-60 age group, and 25 (23.1%) were 60-80.

Qureshi AR et al. studied 231 male patients where age ranged from 14 to 90 years, with a median age of 46 years. All of the patients presented with unexplained shortness of breath. Out of the 231 cases, 12 (5.19%) had cardiac causes, while 219 (94.80%) had non-cardiac

causes. Interestingly, out of the 219 non-cardiac cases, 145 patients (66.21%) were found to have tuberculosis. Among the 145 cases, 69 (47.58%) were diagnosed with active tuberculosis, and 76 (52.41%) were previously treated for tuberculosis and were readmitted due to worsening chest symptoms.(36)

Table 8: Prevalence of pulmonary hypertension in various studies:

Author/Year	Title/Type of study	Sample size	Parameters assessed	Outcomes	Limitations
Bhattacharyya, et al.(45)/(2016)	Tuberculosis associated pulmonary hypertension: The revelation of a clinical observation	40 individuals (21 smokers and 19 non smokers)	Spirometry, echocardiography and radiological evaluation	pulmonary hypertension (PH) seems to be commonly encountered due to various reasons. Interestingly, we found that about 15% of PH patients had a previous history of pulmonary	RHC not done

				tuberculosis as the sole identifiable cause for their condition.	
Rajeev et al.(46) 2020	Pulmonary hypertension in post tuberculosis pulmonary sequelae: attention needed(cross sectional study)	46 patients with sequelae	Echocardiography	21 (45.65%) were found to have pulmonary hypertension, and out of those, 15 (71.43%) also had cor pulmonale	
Mani Tiwari et al(41) 2015	Pulmonary hypertension in pulmonary tuberculosis – a prognostic indicator	728 patients(554(76%) were newly diagnosed with Pulmonary	X ray , echocardiography	Pulmonary TB is strongly correlated with Pulmonary hypertension, which is	

	(observational study)	TB, and 174 (24%) had a previous history of Pulmonary TB)		associated with a poor prognosis. It is essential to diagnose and manage TB early and intervene promptly for pulmonary hypertension. Patients with these conditions typically have a serious prognosis.	
Rohit Chordia et al. (47)(2021)	Clinical profile of pulmonary artery hypertension in treated	30 patients	ECG, echocardiography, X ray	An analytical study was carried out on patients,who were over 18 years old and	

	patients of pulmonary tuberculosis at a tertiary hospital (Cross sectional study)			had been diagnosed with pulmonary artery hypertension (PAH) after receiving treatment for pulmonary tuberculosis (PTB). This study revealed that common echocardiographic changes included right ventricular dilation (63.33%), right atrial dilation (53.33%),	

				inferior vena cava dilation (16.67%), RVH (13.33%), IVS paradoxical motion (6.67%), and pulmonary regurgitation (3.33%). The severity of PAH in the study was categorized as mild (23.33%), moderate (46.67%), and severe (30%).	
Singh G.V. et al.2021	Pulmonary arterial hypertension	94 patients(48	Echocardigraphy,	Among 94 cases that were studied,	

(48)	in patients of healed pulmonary tuberculosis and its association with quality of life	males,46 females)		there were 48 males and 46 females. Out of the 94 patients, 43 had PAH. The prevalence of PAH among cases of healed pulmonary tuberculosis was 45.6%.	
Louw et al 2023	The prevalence of pulmonary hypertension after successful tuberculosis treatment in a community	100 pt	Echocardiography	Only 25% of the participants reported having no lingering symptoms after tuberculosis. Probable	

	sample of adult patients			pulmonary hypertension (PH) was identified in 9% of the participants, while 7% showed borderline elevated pulmonary artery systolic pressure (PASP 35–40mmHg). The study revealed a connection between PH and the number of previous tuberculosis	

				episodes, indicating that each additional episode of tuberculosis raised the odds of post-tuberculosis PH by 2.13-fold.	
Allwood et al 2023(52)	Pulmonary hypertension in adults completing tuberculosis tr eatment	100 patients	Echocardiography, spirometry	One participant was identified with PH (defined as RVSP ≥40 mmHg, and an additional 3 individuals had possible PH (RVSP ≥35 and <40	

				mmHg), resulting in a combined PH prevalence of 4%. Airflow obstruction on spirometry was detected in 13.3% of 98 patients, while 25.5% had a reduced forced vital capacity.	
Kumar, et al 2022(51)	Pulmonary Hypertension in Post-tubercular Pulmonary Fibrosis: A Prospective Study from	80 patients	echocardiography	mild PH was present in 25% of patients, moderate PH in 6.3%, and severe PH in 16.3% of patients. Dyspnea was	

	Western Himalayas			the predominant symptom, reported by all patients, followed by cough (32.5%), hemoptysis (22.5%), chest pain (10%), and syncope (2.5%). Tricuspid regurgitation velocity was below 2.8 m/s in 52.5% of patients, between 2.9 and 3.4 m/s in 30%, and above 3.4 m/s	

				in 17.5% of patients	
Ahmed et al-2011 (53)	Pulmonary Hypertension in patients with Treated pulmonary Tuberculosis: Analysis of 14 consecutive cases (Cross sectional study)	30Patients(14 with pulmonary hypertension)	X ray, Echocardiography,	Out of 30 patients treated for PTB and experiencing shortness of breath, screening was conducted to detect the presence of PH.14of these patients were diagnosed with PH. The average number of years since PTB diagnosis was 9.4. All the had	

				abnormal chest x-rays, with fibrocavitational abnormalities being the most common, occurring in 50% of the patients. Among the patients, 9 (64.3%) had an estimated pulmonary PASP of 51 to 80 mm/Hg, while 4 patients (28.6%) had a PASP of 40 to 50 mm/Hg,	

				and 1 patient had a PASP > 80 mm/Hg	
Jafri S et al 2020(54)	Post Pulmonary Tuberculosis: The Right Heart Story	90 patients	Echocardiography,	Among 90, 80 patients (88.9%) who had pulmonary hypertension (PH), 40 (44.4%) displayed mild, 38 (42.2%) showed moderate, and 2 (2.2%) exhibited severe PH.	
Liu, W., Xu, Y., Yang,	Risk factors for pulmonary arterial	237 Patients	Echocardiography	237 patients with tuberculous	

L. *et al.* *2024* (34)	hypertension in patients with tuberculosis-destroyed lungs and their clinical characteristics compared with patients with chronic obstructive pulmonary disease			destroyed lung (TDL), were split into two groups: 47 patients in the TDL with PH group and 190 in the TDL without PH group. The average age of the patients included in the study was 50.5 ± 17.1 years. In terms of clinical symptoms, individuals in the TDL with PH group experienced a higher	

				occurrence of dyspnea and bilateral lower extremity edema compared to those in the TDL without PH group.(34)	
Jo et al 2017 (55)	Risk factors for pulmonary arterial hypertension in patients with tuberculosis-destroyed lungs and their clinical characteristics compared with patients	195 Patients	Echocardiography	Out of 195 TDL patients, 53 had available echo data, and their average PAP was 50.72±23.99 mmHg. The PAH group (n=37) exhibited reduced lung volume and	

	with chronic obstructive pulmonary disease			more extensively damaged lungs compared to those in the non-PAH group.	

AIM:

"To study the prevalence and risk factors for pulmonary hypertension and myocardial dysfunction in post pulmonary tuberculosis patients of age group 1-18 years"

OBJECTIVE:

Primary

- To study prevalence of pulmonary hypertension in post pulmonary tuberculosis patients of age group 1-18 years.

Secondary

- To study prevalence of myocardial dysfunction in post pulmonary tuberculosis patients age group 1-18 years.
- To assess the risk factors for pulmonary hypertension in post tuberculosis patients of age group 1-18 years.

SAMPLE SIZE CALCULATION-

$$\text{Sample size} = \frac{Z_{1-\alpha/2}{}^2 p(1-p)}{d^2}$$

Z1-a/2 = Is standard normal variate (at 5% type 1 error (P<0.05) it is 1.96 p = Expected proportion in population based on previous studies or pilot studies . d = Absolute error or precision –to be decided by researcher(56)

All children of 1-18 years of age coming to AIIMS OPD under inclusion criteria – sample size calculated from study in India by Bhattacharyya P et al (2018) (5)PTB-related PH made up 15% of all PH cases and precision when taken to be 5% is 196 and when taken 10% is 49.Since our study is a time bound study, we are taking 50 patients as our sample size .

MATERIALS AND METHODS:

STUDY DESIGN AND SAMPLE SIZE:

Single center, cross-sectional study will be conducted in the Department of Pediatrics at All India Institute of Medical Sciences, Bhopal. Institutional human ethics committee approval will be sought before the study. Informed Consent for the study will be obtained from the parents of the patients. This will be time bound study and study will be performed on minimum 50 children and adolescents (age group 1-18 years) with pulmonary tuberculosis who has completed antitubercular treatment within last 1 year.

INCLUSION CRITERIA

- Children and adolescents (age group 1-18 years) with pulmonary tuberculosis .
- Children who has completed anti-tubercular treatment.

EXCLUSION CRITERIA

- Refusal to give consent for the study.
- Patients with structural heart disease.
- Patients with Underlying chronic lung disease other than pulmonary tuberculosis (Obstructive/Restrictive/Airway malformation).
- Patients with extrapulmonary tuberculosis.
- Patients having other systemic illness which are known to increase the risk for pulmonary hypertension (HIV,Sickle cell disease.

METHODOLOGY:

A detailed history of each patient will be taken with special reference to the patient's age, age at diagnosis, clinical symptoms with history of contact and hospital admission will be noted in a predesigned performa. Sputum or gastric aspirate AFB/CBNAAT report whether rifampicin sensitive or resistant along with initial chest x ray and x ray at end of treatment will be collected and assessed. Duration for which antitubercular treatment was taken will be noted. Conventional and TDI echocardiography will be performed in all these cases who has completed treatment and will be noted in a predesigned Performa.

Echocardiographic assessment of Myocardial performance and pulmonary Hypertension

All studies will be performed using Philips EPIQ 7 Color Doppler Ultrasound Machine. All Echocardiograms will be performed by Pediatric cardiologist, who will be blinded regarding the patient clinical diagnosis. An initial scan will be done to rule out structural heart disease.

Variables to be assessed for measuring pulmonary hypertension:

- Estimation of the systolic PAP, through the TR jet velocity by CW Doppler
- Estimation of mean PAP and end-diastolic PAP through CW Doppler of the PR jet
- Pulmonary artery acceleration time (PAAT) RV
- RV myocardial performance (Tei) index

Table 9:Parameters assessed in echocardiography for PH

Parameters assessed	
RV myocardial performance (Tei) index	Increased index predicts RV dysfunction in pediatric PH
PASP (mm Hg)	Bernoulli equation (dP=4×v2): TR velocity used to estimate RVSP (≈PASP) PASP =40-60 mm Hg mild at rest, makes PAH highly likely
Mean PAP (mm Hg)	Estimated mPAP=maximum PR velocity plus mean RAP Def. paediatric PH: mean PAP >25 mm Hg and PVRi >3.0 WU m^2
Diastolic PAP (mm Hg)	Estimated PADP=minimal (end diastolic) PR velocity plus mean RAP PADP independent of RV stroke volume
TR peak velocity (m/s)	RVSP=maximum instantaneous TR gradient across tricuspid valve plus the right atrial v wave. If TR velocity >3.4 m/s, PH is likely
PA acceleration time (ms)	PAAT of <100 ms—high probability of PH

MPI (Myocardial Performance Index) :- It is a numeric value which can be obtained by adding IRT (isovolumetric relaxation time) and ICT (isovolumetric contraction time) of each ventricles.

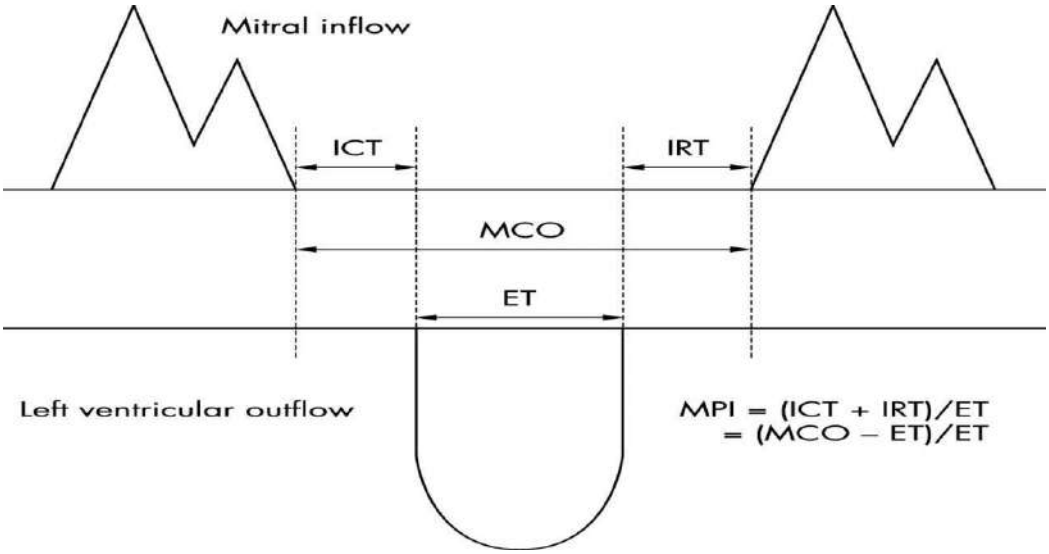


Figure :2 calculation of MPI

Quantification of pulmonary artery systolic pressure:

Tricuspid regurgitation will be assessed in three views: parasternal short-axis, parasternal long axis right ventricular inflow and apical four-chamber to determine a good quality velocity/time wave and the highest velocity obtained from any of the three views was selected as the peak TRV (m/s).

TRV is used to estimate the pulmonary artery systolic pressure using the Bernoulli equation (Pulmonary Artery Systolic Pressure = 4 $(TRV)^2$ + Right Atrial Pressure) .(57)

PHT was defined as peak tricuspid regurgitant jet velocity of ≥2.5m/sec.

Pulmonary hypertension defined as a peak TRV of atleast 2.5 m/second equating to a pulmonary artery pressure of at least 30 mm Hg. Mild pulmonary hypertension defined as peak TRV of 2.5 to 2.9m/second, corresponding to pulmonary artery systolic pressure of 30 to 39 mm Hg.

Moderate pulmonary hypertension defined as a peak TRV ≥ 3 m/second corresponding to pulmonary systolic pressure of 40 to 70mm Hg and severe pulmonary hypertension corresponding to pulmonary artery systolic pressure of >70 mm Hg. Patients with no measurable TRV or TRV <2.5 m/second will be considered to have normal pulmonary artery pressures and normal tricuspid flow.

Masuyama and colleagues (58) showed that the end diastolic pulmonary artery pressure can be calculated accurately using the pulmonary regurgitation jet. From the Bernoulli equation and the peak velocity of the pulmonary regurgitation jet at end-diastole, the diastolic pressure gradient between the pulmonary artery and the right ventricle can be calculated as follows:

$$PADP\text{-}RVED=4\ (V)^2$$

RA pressure is assumed to be equal to RVED pressure, so

$$PADP=RA+4\ (V)^2$$

Using this technique good correlations have been found between Doppler and catheterization measurements of the pulmonary artery-right ventricular end-diastolic pressure gradient (correlation coefficient+0.94, standard error of estimate=3 mm Hg).

If the RA or RVEDP are unknown, pulmonary artery end diastolic pressure can be calculated using a regression equation:

$4 (V)^2=0.61$ PADP-2.0

Similarly peak of the pulmonary regurgitation flow velocity in early diastole correlates well with the mean pulmonary artery pressure (correlation coefficient 0.92, standard error of estimate=5 mm Hg). Using a regression equation that they derived, pulmonary artery mean pressure can be calculated as follows:

$4 (V)^2=0.70$(MPAP)-2

$4 (V)^2$-The peak of all the pulmonary artery to right ventricular diastolic pressure gradient

Pulmonary hypertension will be further confirmed on M-mode across the pulmonary valve (absent a wave, diminished or negative EF slope and mid systolic notch or flutter indicates pulmonary hypertension)

Quantification of Pulmonary artery acceleration time (PAAT) on pulse Doppler tracings across the pulmonary artery: There may be situations in which no tricuspid regurgitation is present or the signal is inadequate to obtain reliable measurements. In these cases it is particularly valuable to look at the PW Doppler signal of pulmonary flow. The normal spectrum is more or less symmetrical in shape. Its maximum velocity is in the range of 0.8 -1.2 m/sec. When pulmonary pressure and pulmonary vascular resistance are high the peak will occur earlier. This can be quantified using the pulmonary velocity acceleration time (PAAT/PVAT). It is the interval between the onset of flow and peak flow.

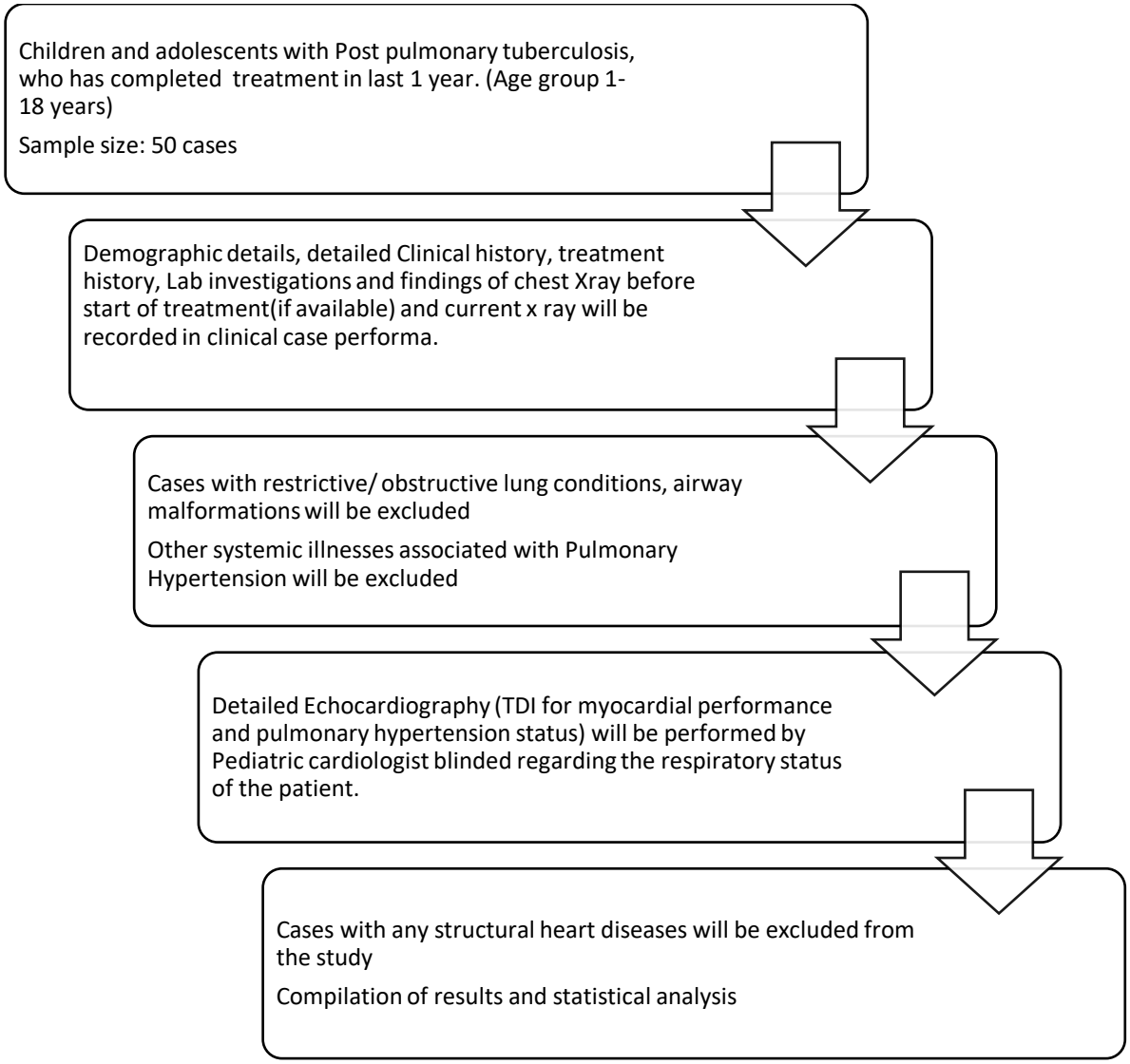
The normal PAAT is > 130 msec.

Using pulmonary acceleration time and the systolic notch one can estimate the severity of pulmonary hypertension on the basis of the following scale:

Severity	PAAT
normal PAP	> 130 msec
borderline PAP	100 - 130 msec
mildly elevated PAP	80 - 100 msec
severely elevated PAP	< 80 msec / systolic notch

Table10: Severity of PAH based on PAAT/PVAT

Figure 3:Study flow diagram


Children and adolescents with Post pulmonary tuberculosis, who has completed treatment in last 1 year. (Age group 1-18 years)
Sample size: 50 cases
Demographic details, detailed Clinical history, treatment history, Lab investigations and findings of chest Xray before start of treatment(if available) and current x ray will be recorded in clinical case performa.
Cases with restrictive/ obstructive lung conditions, airway malformations will be excluded
Other systemic illnesses associated with Pulmonary Hypertension will be excluded
Detailed Echocardiography (TDI for myocardial performance and pulmonary hypertension status) will be performed by Pediatric cardiologist blinded regarding the respiratory status of the patient.
Cases with any structural heart diseases will be excluded from the study
Compilation of results and statistical analysis

Statistical Analysis:

We will use Microsoft Excel for data entry and EPI-Info 7 for data analysis. Descriptive statistics measures i.e, mean and standard deviation will be used to summarize numerical data and percentage for summarizing nominal data. Comparison of categorical data will be done using Chi Square test/Fischer's exact test. The continuous data will be compared by Student's 't' test/Mann Whitney test as applicable. Regression Analysis will be performed.Further,$P<0.05$ will be considered significant.

Timeline:

Table 11: Timeline of study

Period of study	**Achievable targets**
0-6 Months	Case recruitment and clinical assessment of patients
7-9 Months	Protocol to be reassessed for fallacies and minor changes made after discussion with guide. Case recruitment and clinical assessment of patients continued.
10-12 Months	Mid Term analysis shall be done and discussed with guide. Case recruitment and clinical assessment of patients continued.
13-18 months	Case recruitment and clinical assessment of patients continued. Data compilation, statistical analysis, preparation of final report.

RESULTS:

The present study was a cross-sectional study conducted in Department of Paediatrics, AIIMS Bhopal. Fifty children were included in this study fulfilling the inclusion criteria.

Table 12: Demographic details of 50 participants

Details	**Mean±SD /Frequency**
Age (yr)	13.4±4.09
Gender Male Female	 27(54%) 23(46%)
Weight(kg)	142±26.9
Height(cm)	37.6±20
BMI(kg/m2)	16.4±2.99

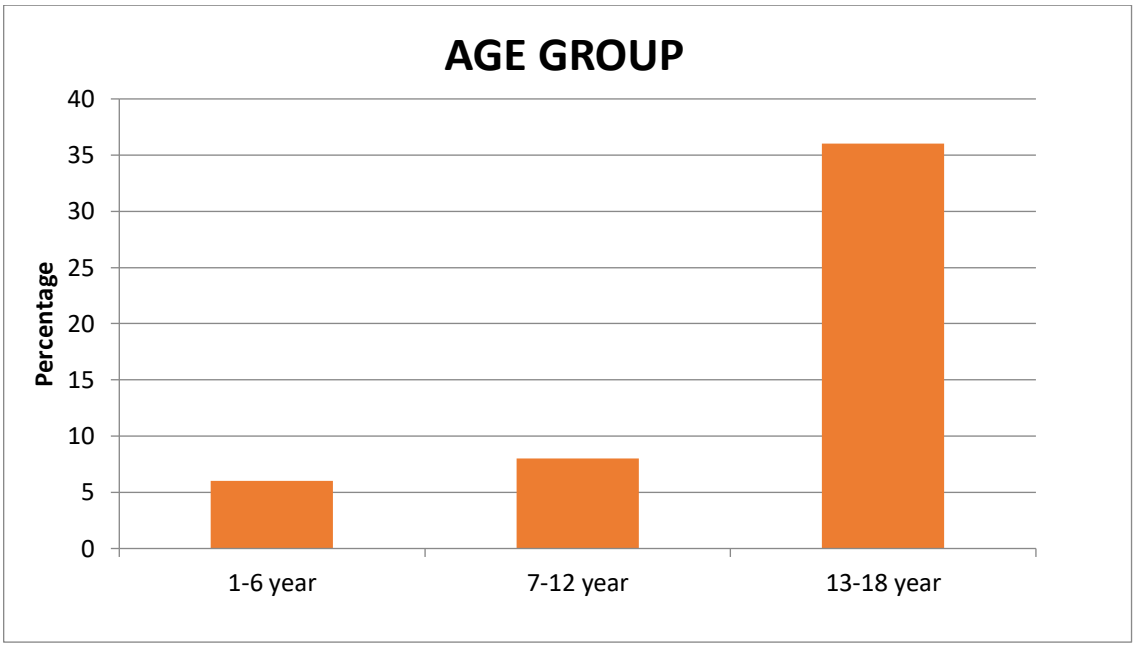
This study included 50 children with history of treatment for pulmonary tuberculosis out of which 27 were males and 23 were females. Male to female ratio of approximately 1.17:1. The mean age of participants was 13.4 ± 4.09. The mean BMI of participants was 16.4 ± 2.99kg/ m2.

Table 13: Distribution of Participants in Terms of Age

AGE	
Mean(SD)	13.4 (4.09)
Median	15
Range	2-18

The mean age of study participants is 13.4 years (SD = 4.09) and the median age is 15 years. Range of participants was between age group of 2 and 18 years.

Figure 4: Distribution of Participants in Terms of Age



Among total 50 patients 6 patient were age group 1-6 years, 8 were in age group 7-12 and most of the patients 38 were in age group 13-18 years

Among 20 patients with pulmonary hypertension mean age was 14.1 years while in patients without pulmonary hypertension was 12.9 years.

Distribution of the participants in terms of Gender

Among the 50 participants, 27(54%) of the participants were males and 23(46%)were females.

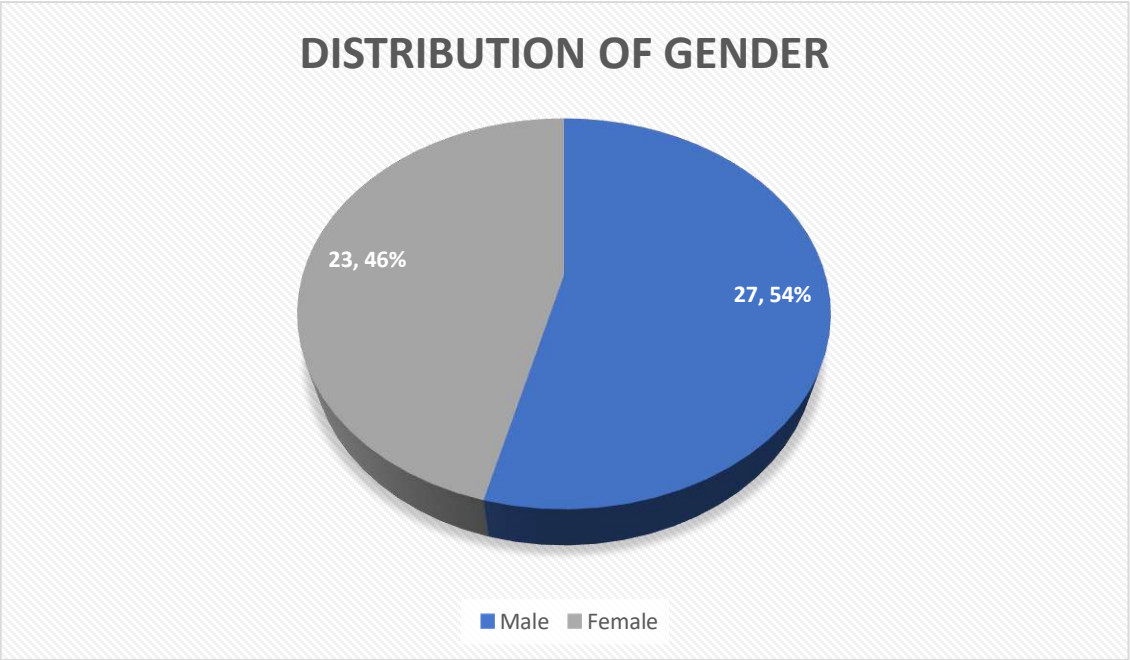


Figure 5: Distribution of gender

Distribution of Participants in Terms of Height

The mean height of the participants was 142 ± 26.9 cm. The median height was 150 cm.

Distribution of Participants in Terms of weight:

The mean weight of the participants was 37.6 kg. The median weight was 34.1kg.

Distribution of Participants in Terms of BMI

The mean BMI of study participants was 16.4 ±2.99 m2 with a range from 10.2 to 22.5.

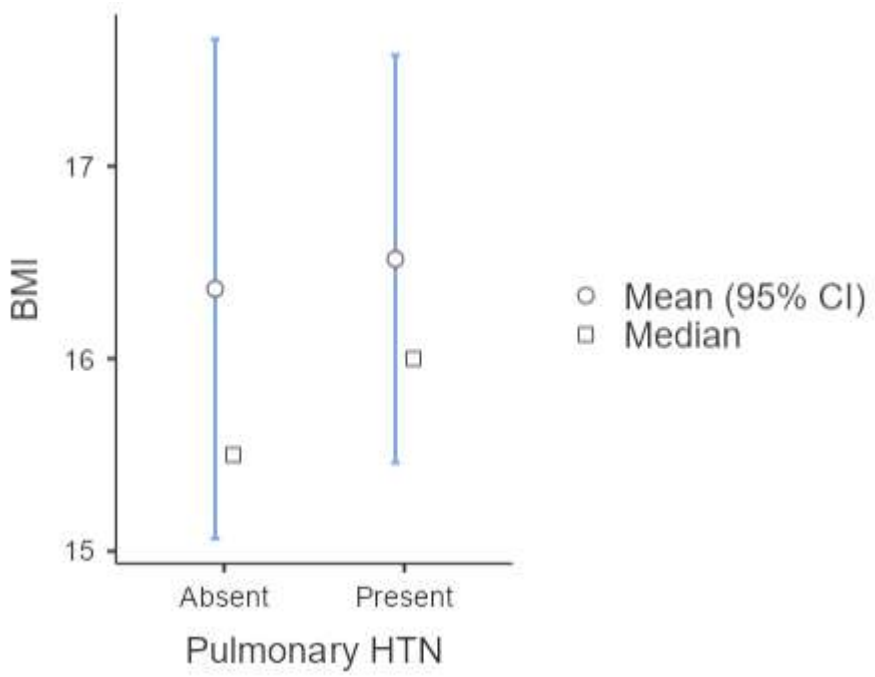


Figure 6 :BMI wise distribution of patient with PH

Distribution of Study participants as per Diagnosis based on AFB/CBNAAT report

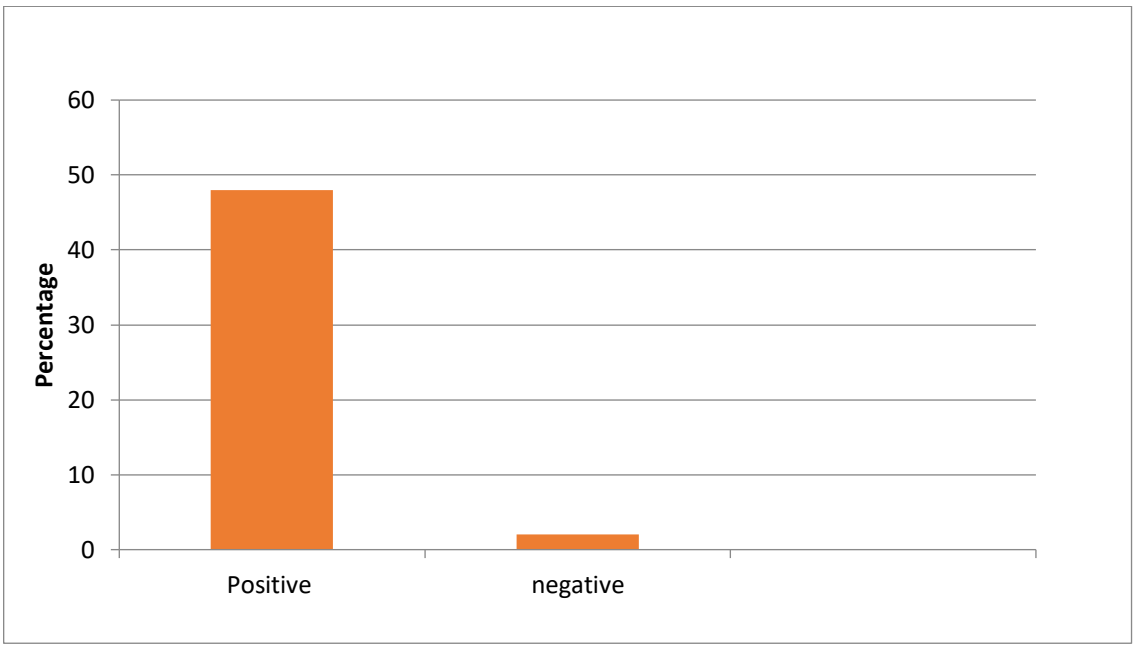


Figure 7: Study participants based on AFB/CBNAAT report

Among 50 patients 48 (96%) patients had positive AFB/CBNAAT report. 2 patients were clinic-radiologically diagnosed.

Distribution of Study participants as per Rifampicin sensitivity report

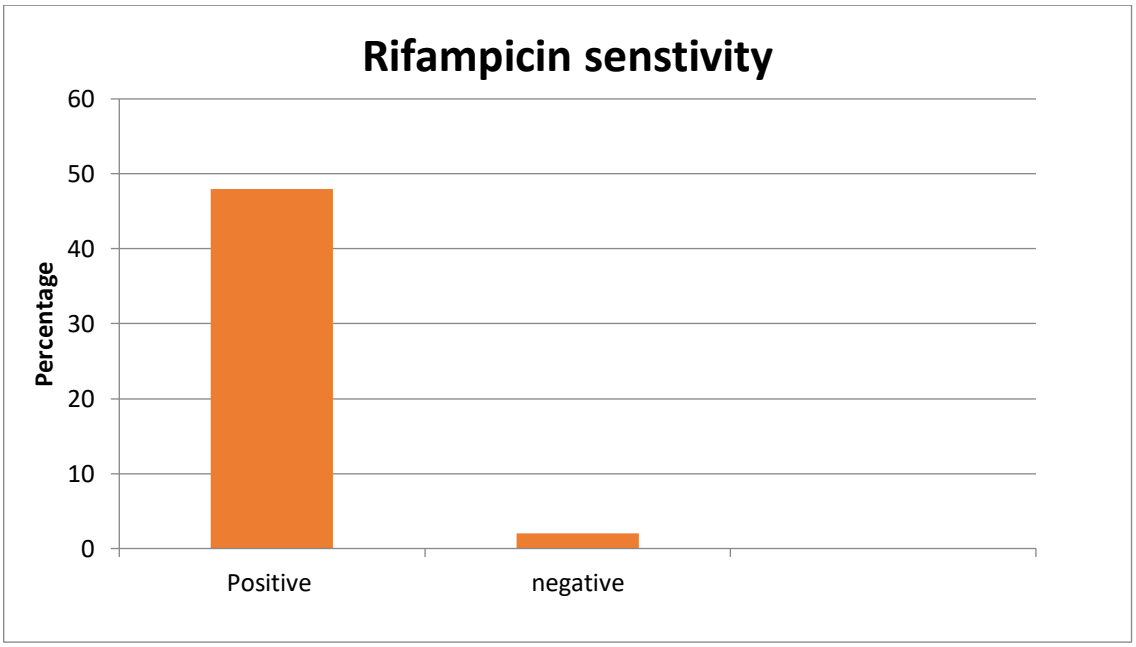


Figure 8:Participants distribution based on Rifampicin sensitivity report

Out of 50 patients 48 (96%) were microbiologically confirmed and all were rifampicin sensitive .

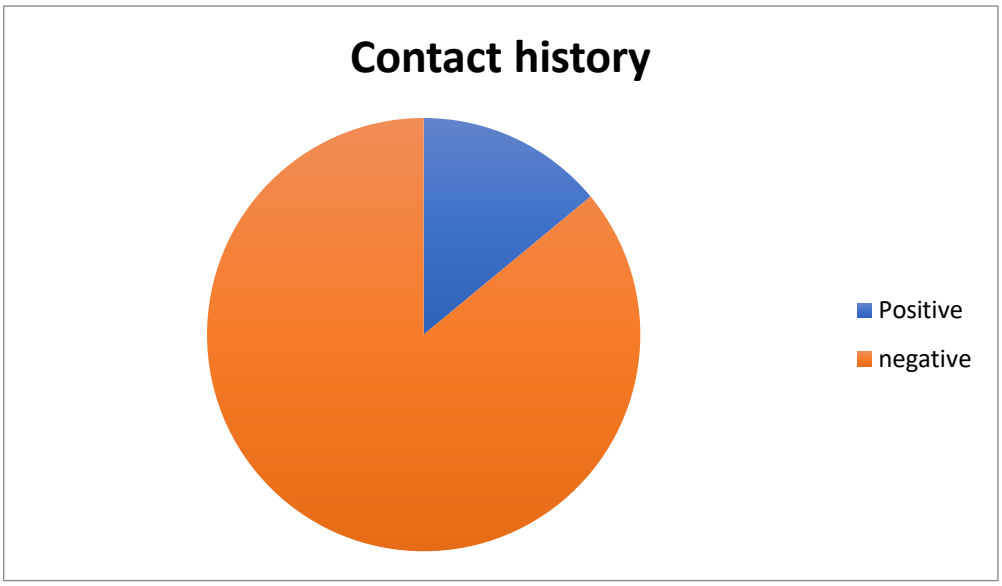
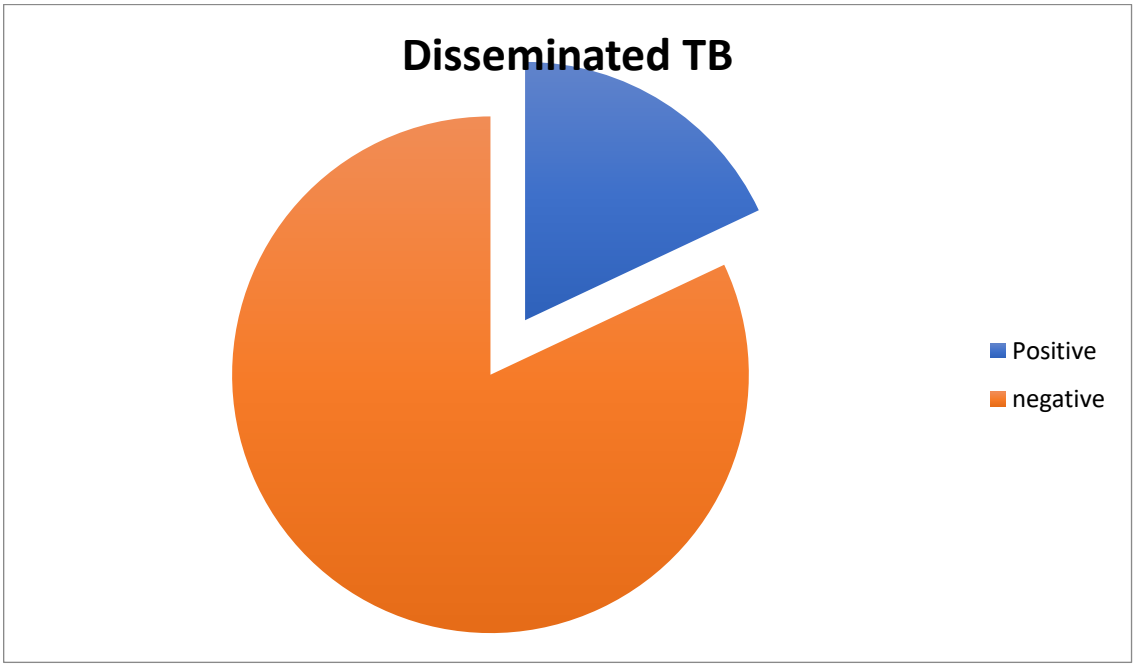


Figure 9: Distribution of participants based on TB contact history:

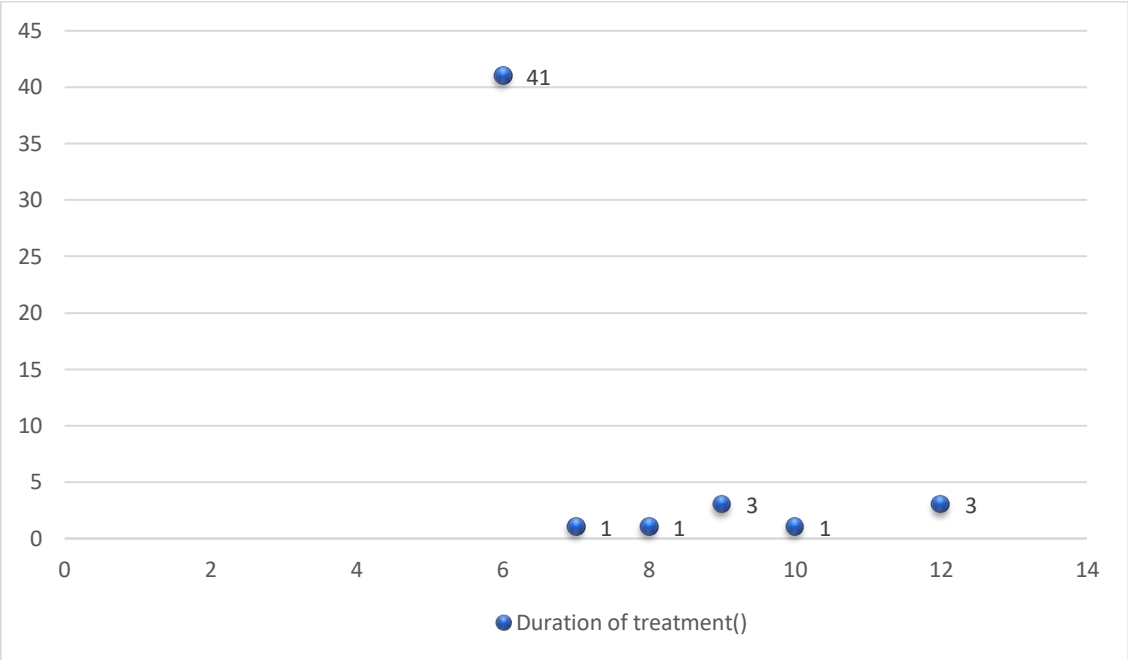
Out of total 50 patients enrolled 7(14%) were having positive history of TB contact prior to illness while 43(86%) patients had no prior contact history.

Figure 10 :Distribution based on disseminated TB:



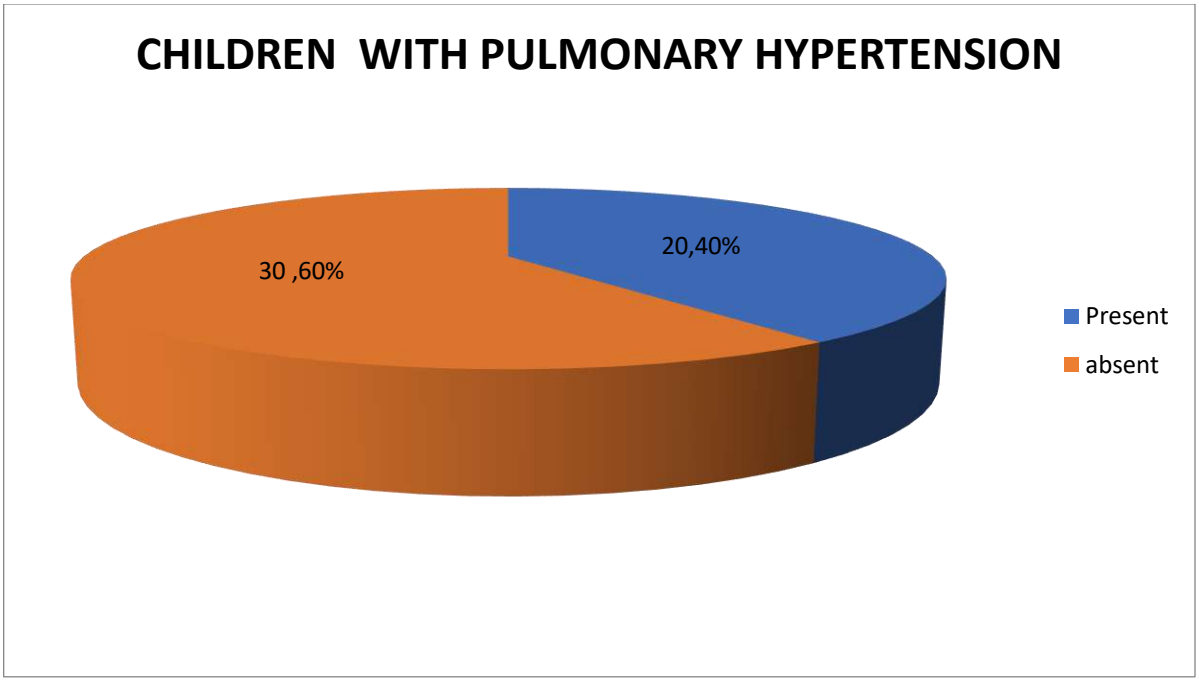
9 (18%) of total assessed patients were found to have involvement of other system along with primary pulmonary illness.

Figure 11:Distribution of patients on basis of duration of anti-tubercular treatment



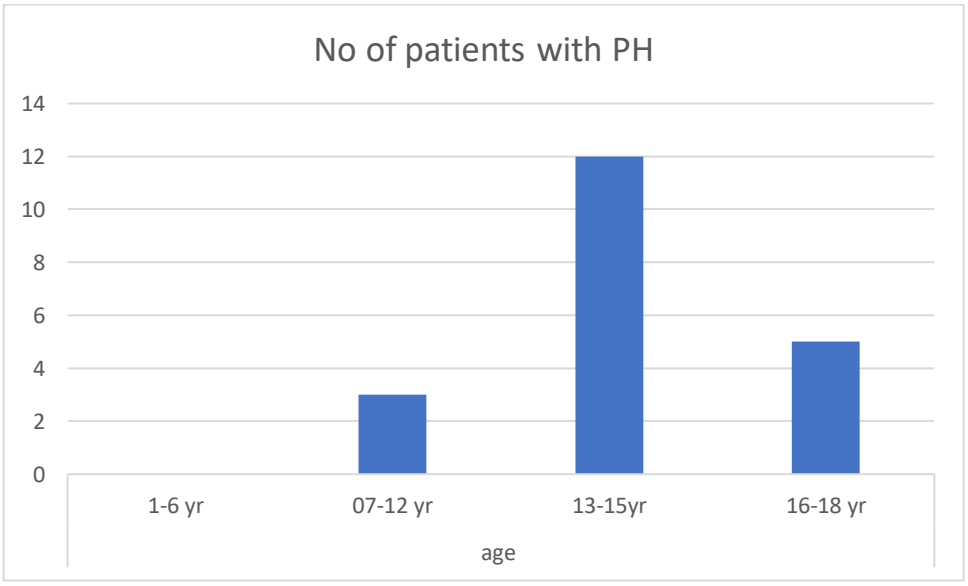
Majority of the patients 41(82%) had taken treatment according to national guidelines with extension of duration of therapy in view of complications during treatment and dissemination of disease.

Figure12: Distribution of patient based on of PH:



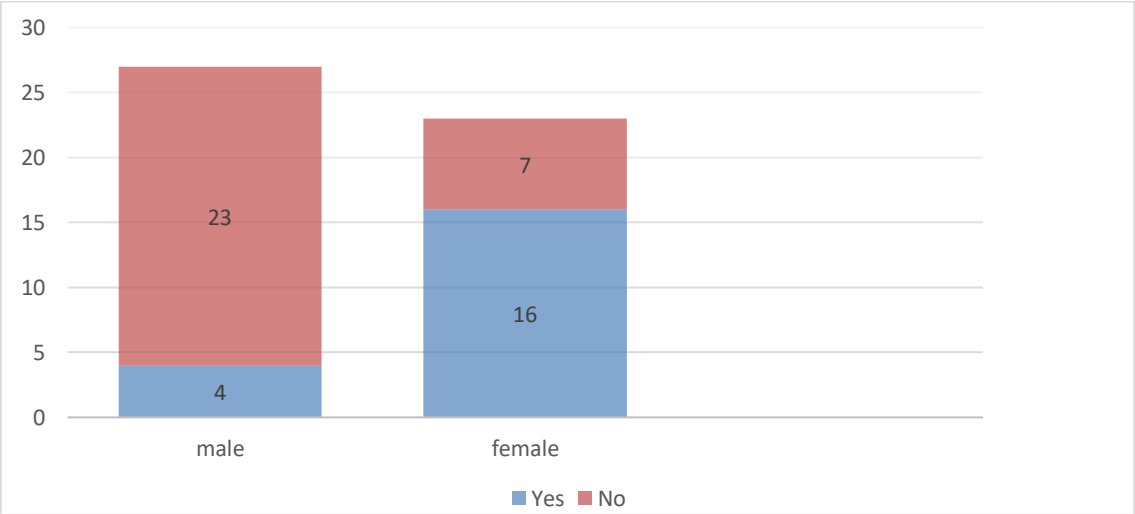
Among the 50 patients with pulmonary TB 20 were found to have PAH, which accounts for 40% of the study population.

Figure 13:Distribution of PH patient according to age



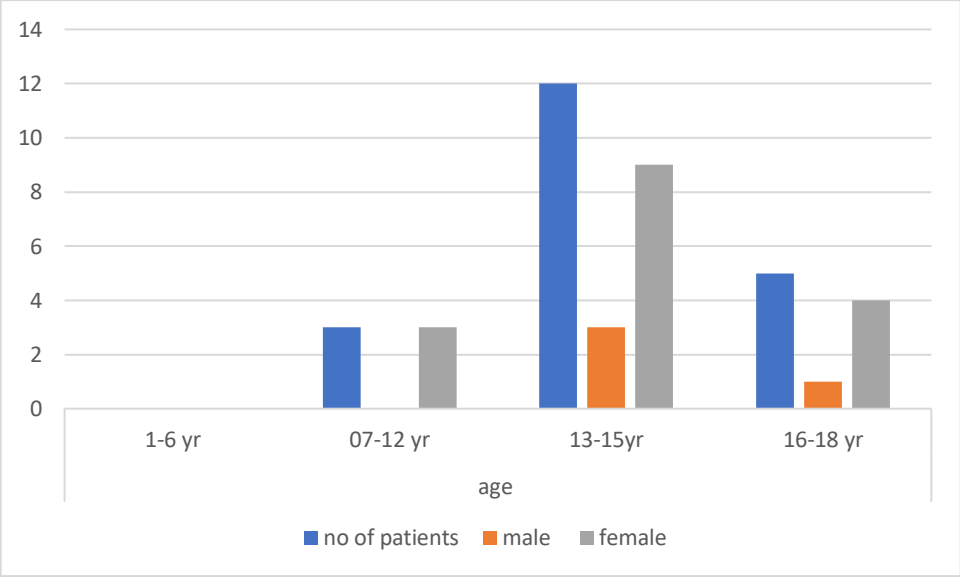
Out of 20 patients of pulmonary hypertension 3 were in age group7-12 years,12 were of age group 13-15 and 5 patients belonged to age group 16-18 years.

Figure 14: Distribution of PH among gender



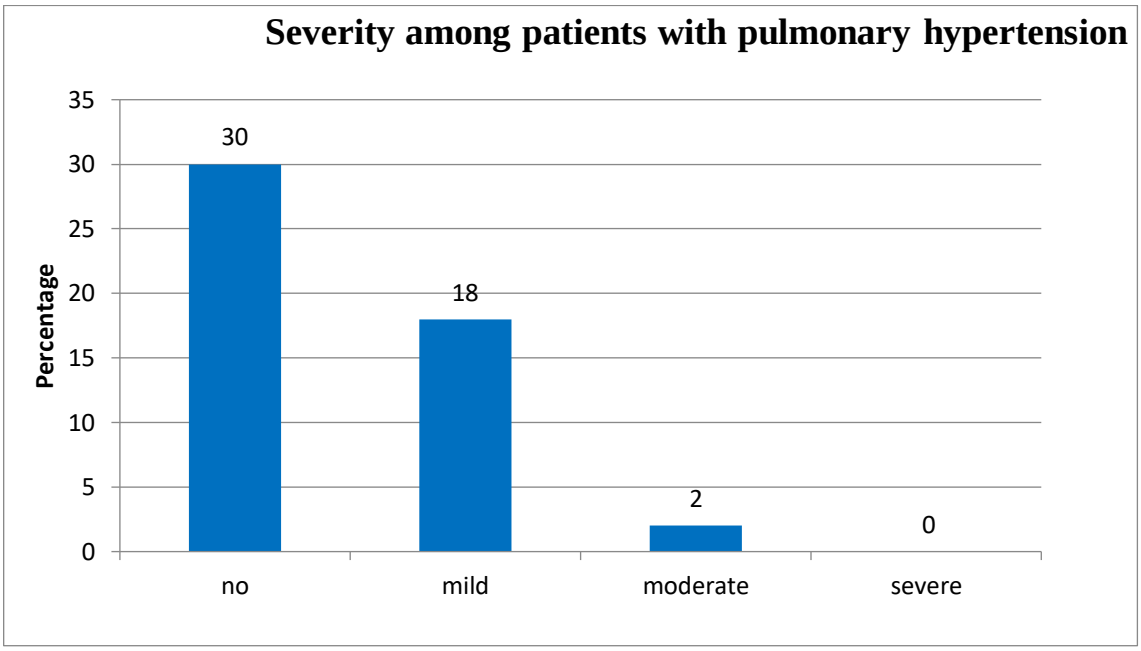
Among 20 patients having pulmonary hypertension 4 were male(20%) while 16 patient were female (80%) .

Figure15:Distribution of patient with PH among age and gender



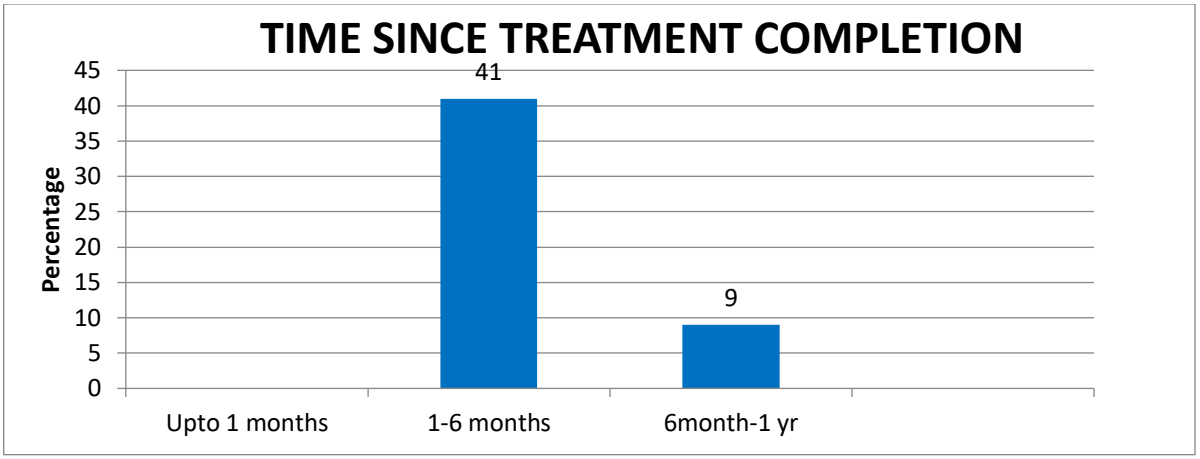
Maximum patients with pulmonary hypertension were in age group 13-15 years with a female preponderance.

Figure16:Distribution of severity of PH



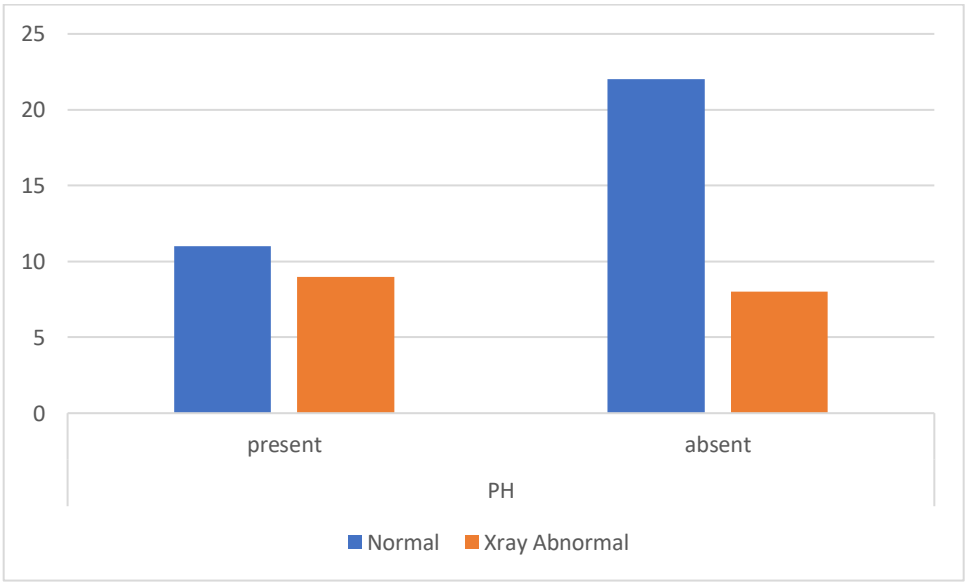
Among total patients (50), 20 (40%) were found to have pulmonary hypertension ,among which the18(90%) patients had mild pulmonary hypertension , while 2 (10%) patients had moderate hypertension

Figure 17:Distribution of patients based on duration since treatment completion



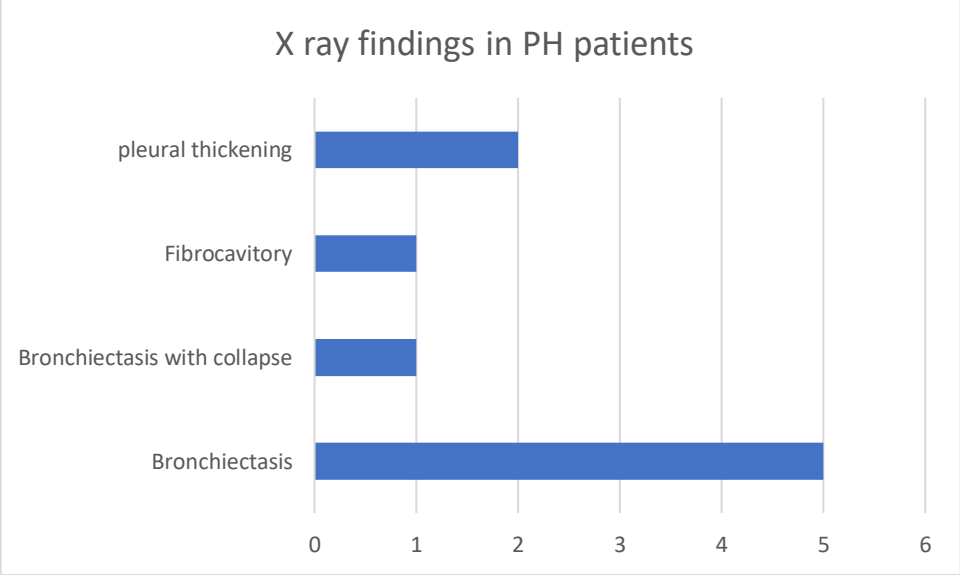
Among 50 patients 41(82%) were evaluated within first 6 months of treatment completion while 9(18%) were evaluated between 6 month till 1 year.

Figure 18 :Distribution of PH among patients based on Xray



Among total 50 patients 33(66%) patients were found to have normal chest x ray findings while 17(34%)were having some abnormality. 11(22%) with normal x ray findings had pulmonary hypertension while 9(18%) patients had x ray abnormalities.

Figure19 :X ray findings in PH patients



Among 9 patients with Xray abnormalities ,6 had residual bronchiectasis changes.

Figure 20:Pulmonary hypertension among patients with previous history of contact

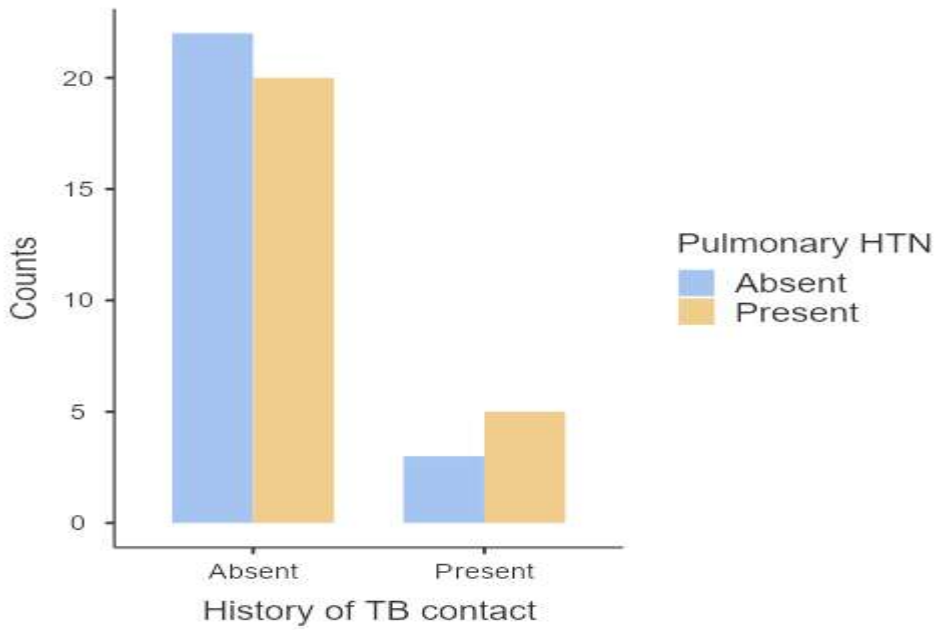
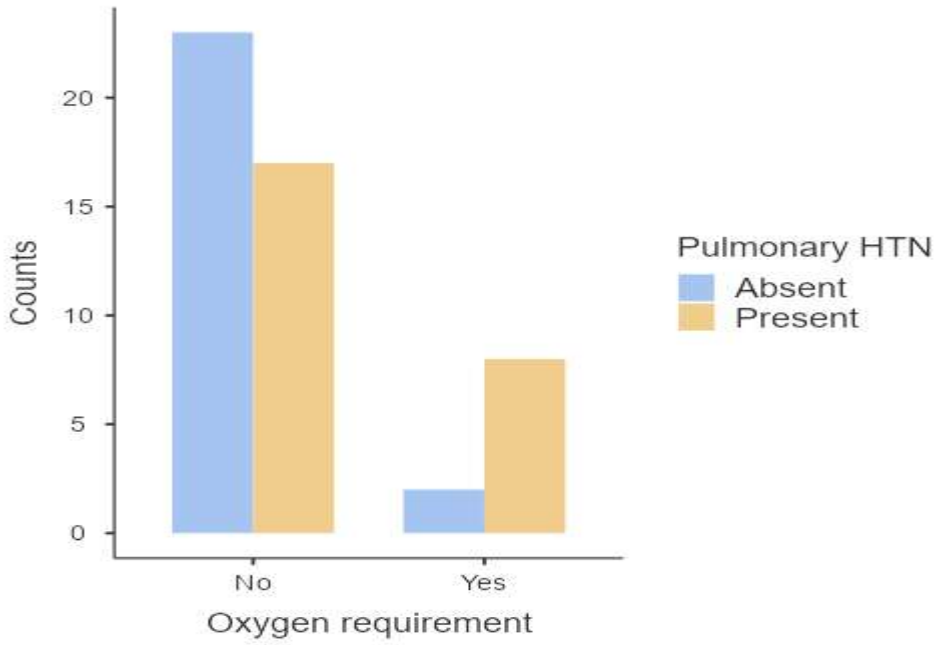


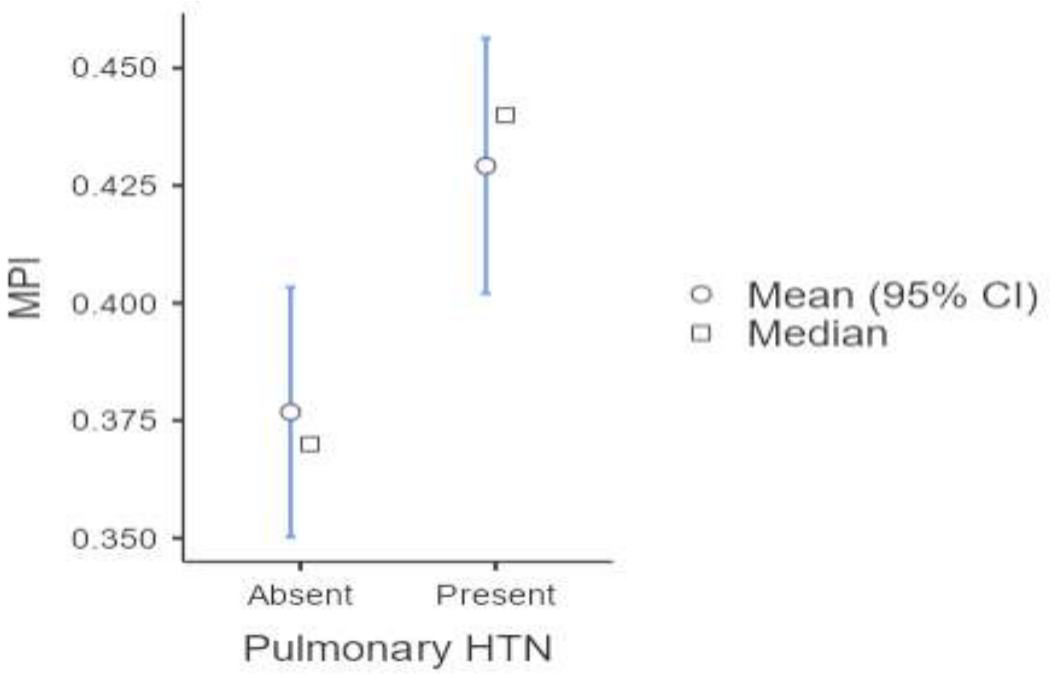
Figure 21:Distribution of PH in patients requiring O2 support during treatment and development of pulmonary hypertension



Oxygen requirement was found in 11(22%) of patients during treatment while 39 patients had no requirement of oxygen support during treatment

DISTRIBUTION OF PATIENTS BASED ON VARIOUS ECHOCARDIOGRAPHY VARIABLES:

Figure 22:Distribution of Mean MPI among patients with or without pulmonary hypertension



Mean MPI calculated for the patients was 0.403 with SD ±0.0728. Median for the patient was 0.4.Among patient group having pulmonary hypertension mean MPI was 0.445 and patients without pulmonary hypertension was 0.375.

TR Gradient and Pulmonary hypertension

Mean TR gradient for the patients was 21 with SD ±10.2.Median for the patient was20,ranging from 6 to 44. Mean TR gradient among patients with PH was 26.1 while in patients without PH was 17.6mmHg.

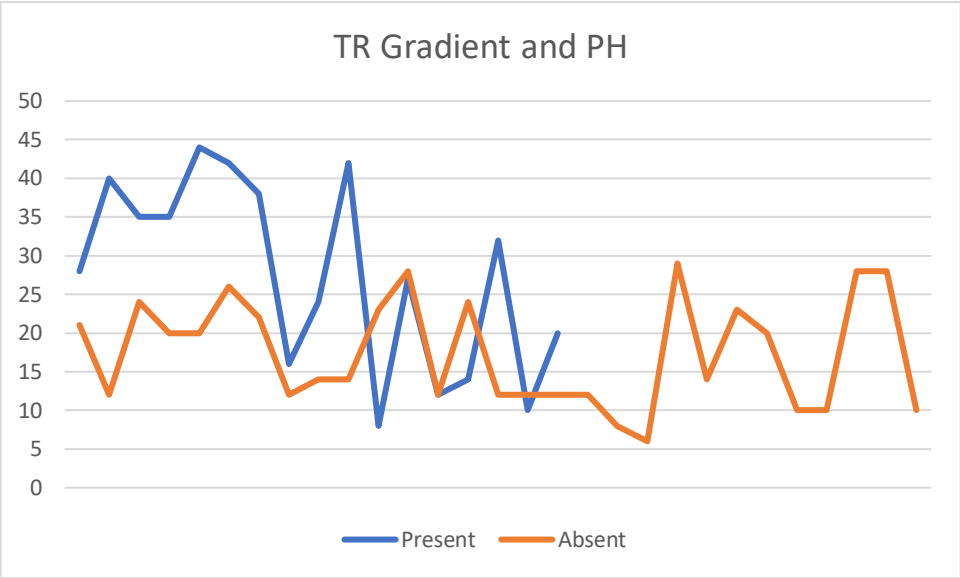


Figure 23: TR gradient and PH

Systolic pulmonary arterial pressure

Mean systolic PAP calculated for the patients was 32 with SD ±10.7.Median for the patient was 31. 8 (40%) out of 20 patients had PASP in range 40-60 mmHg.

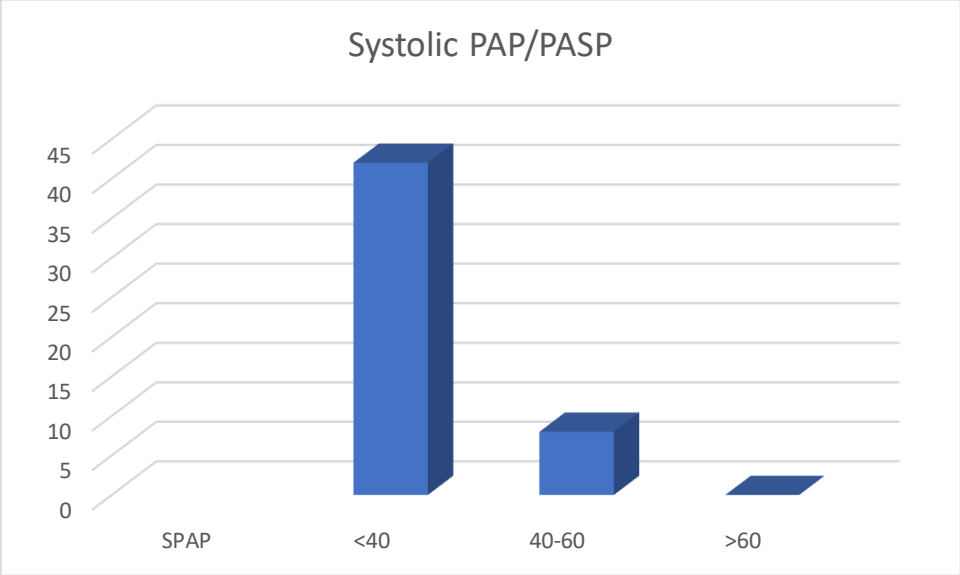


Figure 24: PASP/Spap

PR Gradient among patients with/without PH

Mean PR gradient meaured for the patients was 10.2 with SD ±7.16.Median for the patient was 8 which ranged from 4-32 mmHg.

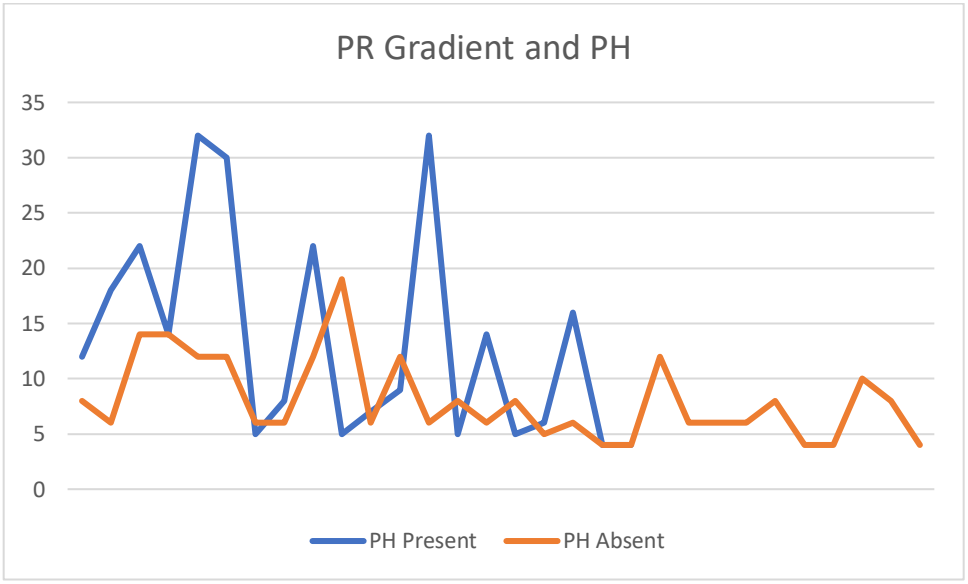


Figure25: PR Gradient and PH

Mean pulmonary arterial pressure:

Mean of mPAP calculated for the patients was 20.2 with SD ±7.16. Median for the patient was 18.

PULMONARY VELOCITY ACCELERATION TIME:

Mean of PVAT/PAAT in patients with pulmonary hypertension was 136 with SD +-13.2 while in patients without pulmonary hypertension it was109 with SD +- 9.81 .

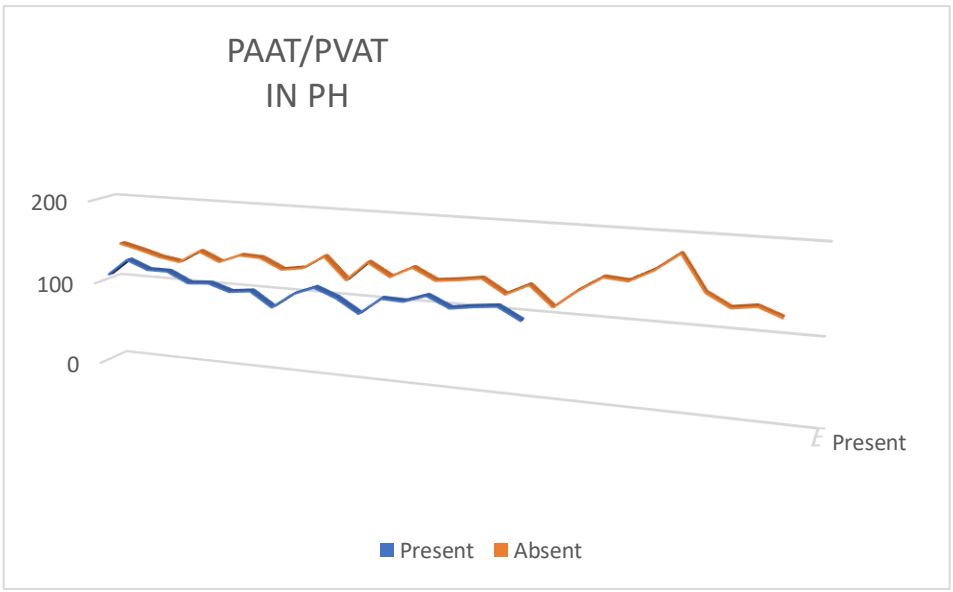


Figure 26:PVAT among patients

Figure 27:Summary of echocardiographic features:

	PULMONARY HTN 1=YES 2=NO	MPI	TR Gradient	Systolic PAP(TR+10)	Peak PR Gradient	Mean PAP(PR+10)	PAAT
Mean	0	0.375	17.6	27.2	8.07	18.1	136
	1	0.445	26.1	37.8	13.5	23.4	109
Median	0	0.385	17.0	24	6.00	16.0	133
	1	0.450	27.5	38.0	10.5	20.0	110
Standard deviation	0	0.0646	7.03	6.17	3.74	3.74	13.2
	1	0.0653	12.1	12.3	9.59	9.62	9.81
Minimum	0	0.300	6	18	4	14	110
	1	0.320	8	18	4	14	88
Maximum	0	0.500	29	38	19	29	180
	1	0.550	44	54	32	42	130

DISCUSSION:

Extensive damage to the lungs is a common outcome of pulmonary TB, leading to increased sickness and death. The development of PH due to chronic lung disease is a major risk factor for worsening respiratory health. Post TB lung disease forms a significant number of chronic lung disease This single center, cross-sectional study was conducted in the Department of Pediatrics at All India Institute of Medical Sciences, Bhopal to study the prevalence of pulmonary hypertension in post pulmonary tuberculosis patients of age group 1-18 years. All children of 1-18 years of age coming to AIIMS OPD under inclusion criteria were included. There are very few studies on PAH in patients with post pulmonary TB. There are limited reports on post TB PH, which has led to its importance being overlooked.

In our study, 50 patients with PTB and lung were included, with 27 being males (54%) and 23 females (46%). The median age of the participants was 15 years. All had completed 6 months of antitubercular therapy following national guidelines. Among the 50 patients with pulmonary TB 20 were found to have PAH, which accounts for 40% of the study population. Of the 20 patients with post-TB PAH, 4(20%) were males and 16(80%) were females. Out of the 20 diagnosed PAH cases, 18(90%) were mild, 2(10%) were moderate, and no patient was having severe PAH based on 2D echocardiography findings.

In a study by Ahmed et al.,(53) out of 30 treated PTB patients, who presented with shortness of breath, 14 (36.6%)were diagnosed to have pulmonary hypertension (PH). Most of them had moderately severe pulmonary hypertension. In our study, out of 50 cases of pulmonary tuberculosis who completed treatment 20 (40%)were found to have pulmonary hypertension

which was similar to the study, but only 2 were found to have moderate pulmonary hypertension and no patient were found to have severe pulmonary hypertension in contrast to the study. Fibrocavitational abnormalities were the most common radiological finding, present in half of the patients. 9 patients (64.3%) had an estimated pulmonary artery systolic pressure (PASP) ranging from 51 to 80 mm/Hg, while 4 patients (28.6%) had PASP between 40 and 50 mm/Hg, and one patient had PASP exceeding 80 mm/Hg. In our study brochiectactic features were predominant in patients of pulmonary hypertension with Xray abnormality and PASP was >40 in 8 (40%)patients of PH.

Another study by Chordia et al. (59)had also revealed revealed fibrocavitation as a common (25%) x ray sequelae post TB .

A research conducted by Bhattacharyya et al.(5) examined 40 patients with pulmonary hypertension (PH) who had previously been treated for pulmonary tuberculosis (PTB). According to the study, PTB-related PH made up 15% of all PH cases. Out of the 40 patients, 21 were smokers, while the remaining 19 were nonsmokers.In our study there was no patient who had history of smoking.

Patel(37) and colleagues conducted an assessment of the causes of PH cases in a civil hospital and identified PTB as the cause in six patients, accounting for 12% of the study population.

In Kumar et al.'s(60) , dyspnea was observed in all 80 patients as the most prevalent symptom, followed by cough (32.5%). Our study also revealed that cough was a common symptom in majority cases .

The frequency of PH in Post TB patients varies across different centers, with reports of 20%–40% of CLD patients, including post TB patients, being affected. The severity of underlying

conditions is related to the occurrence of PH. Our study indicates a PH rate of 40%, falling within the meta-analysis range of 42% for hospitalized or symptomatic patients(61). The high incidence of PH in our study may be due to the high prevalence of TB in India and delayed treatment leading to complications like fibrosis and PH. Studies have highlighted the severity of PH and its association with mortality, with higher mortality reported in individuals with pulmonary artery systolic pressure (PASP) >55 mm Hg. Our study reveals a high percentage of mild PH followed by moderate PH, while a study in another high TB burden country reported PH in 88.9% of patients(54).

Another study from the same country observed 44.4% prevalence among 108 patients and the severity of PH ranged from mild to severe, with fewer cases of mild PH possibly due to limited hospital visits for mild symptoms in remote mountainous areas. (62)Previous studies have used electrocardiography or postmortem examination for diagnosing PH and cor pulmonale, with most patients receiving proper chemotherapy for TB treatment. In our study, doppler echocardiography was utilized for diagnosing PH, which is considered the best non-invasive method for such diagnosis. The prevalence of PH was higher in females, with 14% male and 69.5% female patients affected in our study.

Included in the study by Qureshi et al(63) were 231 consecutive cases with a clinical and radiological suspicion of pulmonary hypertension and an age greater than 14 years. Among these cases, 69 out of 231 (29.87%) had active tuberculosis, while 76 out of 231 (32.90%) had been treated for tuberculosis in the past. Major risk factors included cigarette smoking, diabetes mellitus, and obesity.

Patients with a history of pulmonary tuberculosis and bronchiectasis were nearly always linked with pulmonary hypertension, indicating that post-infectious complications are a

significant factor in the development of pulmonary hypertension.(64).With similar findings in our study severity of extention of lung destruction can be a contributing factor for development of PH in post TB patients.

Study done by Sharma et al(51) with 80 patients showed 25% had mild PH,6.3 %had moderate and 16.3% had severe PH with total prevalence of 47.6% as compared to our 40% total prevalence.

While assessing the quality of life in post TB patients involving total of 94 cases, with 48 being males and 46 being females. Among the 94 patients, 43 were diagnosed with PAH. The prevalence of PAH among individuals with a history of healed pulmonary tuberculosis was found to be 45.6%.(48) which was similar to the results compared with our study.

Pulmonary hypertension was found to be prevalent in 60.66% of cases.(65) Their analysis showed a significant link between BMI, smoking habits, diabetes, sensitivity to medication, and spirometry results. Among patients, fibrosis was the most common type of pulmonary TB sequelae, followed by bronchiectasis (18.85%), cavity (9.83%), bullae (6.55%), aspergilloma (4.91%), and pleural thickening and calcification (4.09%).There were similar findings observed in our patients with bronchiectasis (30%)and pleural thickening (10%) .

PH was mild in 29%,moderate in 22.9% and severe in 8.19% and normal in 39.3% while in our study it was mild in 36% of total patients and moderate in 4%.

The connection between the years of treatment completed for PTB and PAH is an important concern that has not been addressed before.

A study conducted by (37)on 100 patients, with the average (±SD) pulmonary arterial hypertension (PAH) being 60 (±10) mmHg and ranging from 44 to 84 mmHg. The majority of the cases exhibited moderate PAH.(37) In our study Mean systolic PAP calculated for the patients was 32with SD ±10.7.Median for the patient was 31and majority (90%)of patients had mild PH.

Louw et al.(66) measured average PASP 29mmHg in 99 individuals. Probable PH-postTB was detected in 9 participants, resulting in a prevalence of 9%. Additionally, seven individuals (7%) exhibited borderline elevated PASP levels ranging from 35 to 40mmHg. In this study, 4 patients had PASP values exceeding 50mmHg. A significant link was established between probable PH and the number of previous TB episodes, with each additional episode increasing the odds of probable PH-postTB by 2.13 times. Symptoms such as cough, sputum, wheezing, and dyspnea showed no correlation with probable PH.

The study not only demonstrated the connection between pulmonary hypertension and tuberculosis, but also emphasized that tuberculosis is frequently the main cause of pulmonary hypertension in populations with high disease burdens, often overlooked as the cause of pulmonary hypertension. It is evident from this conversation that pulmonary hypertension is linked to higher morbidity, mortality, and reduced quality of life. The key to avoiding unfavorable outcomes is early diagnosis and timely treatment.

SUMMARY:

- This is a single centre cross sectional observational study conducted in the outpatient department of Department of Pediatrics, AIIMS Bhopal.
- A total of 50 patients were assessed during the study period.
- 40% (20 /50) of the study population was found to have pulmonary hypertension, out of which 10% (2 /20)was found to have moderate PAH and 90%(18/20) of the children were found to have mild PAH.
- This is a pilot study in pediatric population assessing the prevalence of pulmonary hypertension in post pulmonary TB patients Very few studies are present evaluating post TB patients for pulmonary hypertension in adult patient often complicated with other comorbid conditions.
- The study found a high prevalence of post-TB PH, but TB or PTLD is seldom mentioned in the existing PH literature as cause.

CONCLUSION:

- In populations with a high prevalence, pulmonary tuberculosis can be the main cause of pulmonary hypertension.
- The impact of post-TB PH on communities is currently not well understood but is probably significant.
- It is important to accurately determine the prevalence by studying a large number of patients who have been previously treated for TB.
- Echocardiography is a good tool for evaluation of pulmonary hypertension and follow up.

LIMITATIONS:

- Limited sample size
- This is a single centre study conducted in AIIMS Bhopal, a tertiary health care system,
- Cross- sectional nature of the study.
- Echocardiography report before the start of treatment was not available.
- ECG correlation in patients with pulmonary hypertension was not done.
- Nutritional status and BMI should have also been considered.
- The value of PH has not been verified through right heart catheterization, which is considered the gold standard method.
- All the patients were of drug sensitive TB and no DRTB could be enrolled in this study

FUTURE SCOPE:

- There is a need for research to establish the time between the initial TB episode and the onset of PH, as this could have significant implications for ongoing monitoring, screening, and treatment.
- Due to high prevalence of pulmonary hypertension ,routine ECHO based screening should be considered in post TB patients.

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ANNEXURES:

PROFORMA

Name :

Age/Sex :

UHID no :

Father's Name :

Mother's Name :

Address :

Contact No. :

History :

- Age at diagnosis
- Symptoms at the time of diagnosis
    - AFB/CBNAAT report
    - Chest X- ray
- History of fever.(Y/N)
- History of chronic cough. .(Y/N)
- History of weight loss. .(Y/N)
- History of night sweats. .(Y/N)
- Shortness of breath. (Y/N)
- Respiratory distress. .(Y/N)
- Decreases physical exercise. .(Y/N)
- Family History:
    - Any member of the family suffering from similar illness, (with description)
    - Family history of pulmonary hypertension.

Hospitalisation history(if applicable)

- Age at first hospital admission due to symptoms-
- Number of hospital admissions-

Treatment History

- Age at starting treatment.
- Duration of treatment.
- Oxygen requirement.
- Any other drug history

Anthropometry:

- Weight(kg)
- Height(cm)
- BMI(kg/m2)

General examination:

- P/I/Cl/Cy/Ed/LN:
- Blood pressure(age appropriate centiles):
- SpO_2
- RR(cpm)

Physical Examination:

- Inspection
- Palpation
- Auscultation

Investigations :

- CBC
  - ✓ Hb:
  - ✓ RBC Counts
  - ✓ TLC
  - ✓ DLC(N/L/M/E/B)
  - ✓ Platelets
- LFT

  T/D/ I Bilirubin

AST/ALT

- AFB/CBNAAT report
- Chest Radiograph
- Any other:

Immunisation status:

- Routine immunization as per NIS
- Any other

ECHOCARDIOGRAPHY

- Structurally Normal/Abnormal
- MPI
- TR Gradient:
- Early diastolic peak PR gradient:
- End Diastolic Peak PR gradient:
- Pulmonary artery acceleration time:
- M Mode across Pulmonary valve:

Interpretation:

अखिल भारतीय आयुर्विज्ञान संस्थान भोपाल

All India Institute of Medical Sciences Bhopal

Assent Form

Dear participant

We are doing a study on "**To study the prevalence and risk factors for pulmonary hypertension and myocardial dysfunction in post pulmonary tuberculosis patients of age group 1-18 years''**

We are asking you for registering in this study as this will help in studying the prevalence and risk factors of pulmonary hypertension and myocardial dysfunction in post tuberculosis patients

You can ask questions about this study at any time. If you decide at any time not to participate, you can ask us to stop.

If you sign this paper, it means that you have read this and that you want to be in the study. If you don't want to be in the study, don't sign this paper. Being in the study is up to you, and no one will be upset if you don't sign this paper or if you change your mind later.

Your signature: _____

Date_____

Your printed name: _____

Signature of person obtaining consent with date: _____

Printed name of person obtaining consent: _____

Date _____

अखिल भारतीय आयुर्विज्ञान संस्थान भोपाल

All India Institute of Medical Sciences Bhopal

प्रिय प्रतिभागी

हम "1-18 वर्ष आयु वर्ग के पोस्ट पल्मोनरी टीबी रोगी में पल्मोनरी हाइपरटेंशन और मायोकार्डिअल डिसफंक्शन के प्रसार और जोखिम कारकों का अध्ययन करने के लिए" पर एक अध्ययन कर रहे हैं।

हम आपसे इस अध्ययन में पंजीकरण करने के लिए कह रहे हैं क्योंकि इससे टीबी के बाद के रोगियों में पल्मोनरी हाइपरटेंशन और मायोकार्डिअल डिसफंक्शन के प्रसार और जोखिम कारकों का अध्ययन करने में मदद मिलेगी।

आप किसी भी समय इस अध्ययन के बारे में प्रश्न पूछ सकते हैं। यदि आप किसी भी समय भाग न लेने का निर्णय लेते हैं, तो आप हमें रुकने के लिए कह सकते हैं।

यदि आप इस कागज़ पर हस्ताक्षर करते हैं, तो इसका अर्थ है कि आपने इसे पढ़ लिया है और आप अध्ययन में बने रहना चाहते हैं। यदि आप अध्ययन में नहीं रहना चाहते हैं, तो इस पेपर पर हस्ताक्षर न करें। अध्ययन में बने रहना आप पर निर्भर है, और यदि आप इस पेपर पर हस्ताक्षर नहीं करते हैं या बाद में अपना विचार बदलते हैं तो कोई भी परेशान नहीं होगा।

आपका हस्ताक्षर: _____

तारीख_____

आपका नाम: _____

दिनांक के साथ सहमति प्राप्त करने वाले व्यक्ति के हस्ताक्षर: _____

सहमति प्राप्त करने वाले व्यक्ति का नाम: _____

तारीख _____

अखिल भारतीय आयुर्विज्ञान संस्थान भोपाल

All India Institute of Medical Sciences Bhopal

Participant Information Sheet(for assent in pediatric population)

1. STUDY TITLE: To study the prevalence and risk factors for pulmonary hypertension and myocardial dysfunction in post pulmonary tuberculosis patients of age group 1-18 years

2. STUDY INVESTIGATORS:

3. Student: Dr Shubham, Department Of Pediatrics

4. Guide: Dr Amber Kumar, Department Of Pediatrics

5. Co- Guides

Prof (Dr)Shikha Malik , Department Of Pediatrics

Dr Bhavna Dhingra, Department Of Pediatrics

6. Introduction:

We are conducting a research study to study the prevalence and risk factors of pulmonary hypertension and myocardial dysfunction in post tuberculosis patients in AIIMS Bhopal. We would like you to be a part of this study. If you agree to take part voluntarily, we will ask you to sign a consent form.

7. Purpose of the study:

The aim of our study is to study prevalence of pulmonary hypertension in post pulmonary tuberculosis patient of age group 1-18 years

Taking part – what it involves:

a. Do I have to take part?

Participation in this research is entirely voluntary. A decision to not take part, or to withdraw at any time, will not affect your rights or medical care in any way.

b. What is expected of me if I take part?

If you participate, we will collect information about the patient and perform echocardiography

How long will my part in the study last?

Your participation in the study would last for single visit

c. Do I have to come for extra visits or undergo extra investigations for the study?
Echocardiography will be done on routine follow up. No extra investigations or visits required for the same

d. What are the possible benefits in taking part?
Taking part will help gain knowledge about the disease and possible complications
What are the possible disadvantages and risks of taking part?
There are no major foreseeable disadvantages or risks because of the study. There may be risk of loss of privacy and confidentiality of information collected even though all possible measures will be taken to ensure safe data storage and access.

e. What happens to the information collected from me?
All information collected will be kept strictly confidential and not shared with anyone. Results from the study will be reported as group data and will not identify you in any way.

f. What if I change my mind regarding participation in the study?
You are entitled to change your mind and withdraw at any time during the study without any disadvantage or penalty.

g. Whom do I contact for more information or if I have further questions or concerns?
If you want any information or have questions or concerns, you can contact:

Dr. Shubham
Post graduate student,
Department of Pediatrics , AIIMS, Bhopal
(8814016049,yadavshubham.sm@gmail.com)

Dr. Shashank Purwar
Member Secretary,
Institute Ethics Committee-StudentResearch
(7773010099,ihecpgr@aiimsbhopal.edu.in)

अखिल भारतीय आयुर्विज्ञान संस्थान भोपाल

All India Institute of Medical Sciences Bhopal

प्रतिभागी सूचना पत्रक

1. अध्ययन शीर्षक: 1-18 वर्ष आयु वर्ग के पोस्ट पल्मोनरी टीबी रोगी में पल्मोनरी हाइपरटेंशन और मायोकार्डिअल डिसफंक्शन के प्रसार और जोखिम कारकों का अध्ययन करने के लिए

2. अध्ययन अन्वेषक:

3. छात्र : डॉ. शुभम, बाल रोग विभाग

4. मार्गदर्शक: डॉ. अंबर कुमार, बाल रोग विभाग

5. सह-गाइड

प्रो (डॉ) शिखा मलिक, बाल रोग विभाग

डॉ भावना ढींगरा, बाल रोग विभाग

6. परिचय:

हम एम्स भोपाल में टीबी के बाद के रोगियों में पल्मोनरी उच्च रक्तचाप और मायोकार्डियल डिसफंक्शन के प्रसार और जोखिम कारकों का अध्ययन करने के लिए एक शोध अध्ययन कर रहे हैं। हम चाहते हैं कि आप इस अध्ययन का हिस्सा बनें। यदि आप स्वेच्छा से भाग लेने के लिए सहमत हैं, तो हम आपसे एक सहमति फॉर्म पर हस्ताक्षर करने के लिए कहेंगे।

7. अध्ययन का उद्देश्य:

हमारे अध्ययन का उद्देश्य 1-18 वर्ष आयु वर्ग के पोस्ट पल्मोनरी टीबी रोगी में पल्मोनरी हाइपरटेंशन के प्रसार का अध्ययन करना है

8. भाग लेना - इसमें क्या शामिल है:

a. क्या मुझे भाग लेना है?

इस शोध में भागीदारी पूरी तरह से स्वैच्छिक है। भाग न लेने या किसी भी समय वापस लेने का निर्णय किसी भी तरह से आपके अधिकारों या चिकित्सा देखभाल को प्रभावित नहीं करेगा।

b. यदि मैं भाग लेता हूँ तो मुझसे क्या अपेक्षा की जाती है?

यदि आप भाग लेते हैं, तो हम रोगी के बारे में जानकारी एकत्र करेंगे और इकोकार्डियोग्राफी करेंगे

C अध्ययन में मेरा हिस्सा कितने समय तक चलेगा?

अध्ययन में आपकी भागीदारी एक मुलाक़ात तक चलेगी

d. क्या मुझे अध्ययन के लिए अतिरिक्त मुलाकातों या अतिरिक्त जांचों के लिए आना होगा?

नियमित फॉलोअप पर इकोकार्डियोग्राफी की जाएगी। इसके लिए किसी अतिरिक्त जांच या दौरे की आवश्यकता नहीं है

e. भाग लेने के संभावित लाभ क्या हैं?

भाग लेने से बीमारी और संभावित जटिलताओं के बारे में ज्ञान प्राप्त करने में मदद मिलेगी

f. भाग लेने के संभावित नुकसान और जोखिम क्या हैं?

अध्ययन की वजह से कोई बड़ा अनुमानित नुकसान या जोखिम नहीं हैं। एकत्र की गई जानकारी की गोपनीयता और गोपनीयता के नुकसान का जोखिम हो सकता है, भले ही सुरक्षित डेटा भंडारण और पहुंच सुनिश्चित करने के लिए सभी संभव उपाय किए जाएंगे।

g. मुझसे एकत्र की गई जानकारी का क्या होता है?

एकत्र की गई सभी सूचनाओं को कड़ाई से गोपनीय रखा जाएगा और किसी के साथ साझा नहीं किया जाएगा। अध्ययन के परिणाम समूह डेटा के रूप में रिपोर्ट किए जाएंगे और किसी भी तरह से आपकी पहचान नहीं करेंगे।

h. क्या होगा अगर मैं अध्ययन में भाग लेने के बारे में अपना विचार बदल दूं?

आप अपना विचार बदलने और अध्ययन के दौरान किसी भी समय बिना किसी नुकसान या दंड के वापस लेने के हकदार हैं।

i. अधिक जानकारी के लिए या मेरे और प्रश्न या चिंताएँ होने पर मैं किससे संपर्क करूँ?

यदि आप कोई जानकारी चाहते हैं या आपके कोई प्रश्न या चिंताएँ हैं, तो आप संपर्क कर सकते हैं:

डॉ। शुभम
स्नातकोत्तर विद्यार्थी,
बाल रोग विभाग, एम्स, भोपाल
(8814016049,yadavshubham.sm@gmail.com)

डॉ. शशांक पुरवार
सदस्य सचिव,
समिति - छात्र अनुसंधान संस्थान नैतिकता
(7773010099,ihecpgr@aiimsbhopal.edu.in)

अखिल भारतीय आयुर्विज्ञान संस्थान भोपाल

All India Institute of Medical Sciences Bhopal

प्रतिभागी सूचना सहमति प्रपत्र
[PARTICIPANT INFORMED CONSENT FORM (PICF)]

इस अध्ययन के लिए प्रतिभागी का पहचान नंबरः .....
Participant Identification Number for this Study: .....

अनुसंधान का शीर्षकः **To study the prevalence and risk factors for pulmonary hypertension and myocardial dysfunction in post pulmonary tuberculosis patient of age group 1-18 years**

शोधकर्ता छात्र का नाम - डॉ शुभम फोन नं:-8814016049
शोध मार्गदर्शक का नाम : डॉ अंबर कुमार

मैंने दिनांक 20.08.2022 के सूचना पत्रक संस्करण II में दिए गए सभी तथ्यों को सावधानीपूर्वक पढ़ लिया है/ मुझे अपनी भाषा में स्पष्ट रूप से विस्तारपूर्वक समझा दिया गया है, और मैंने तथ्यों को पूर्णतः समझ लिया है। मैं पुष्टि करता/ करती हूँ, कि मुझे सवाल पूछने के अवसर प्रदान किए गए। The contents of the information sheet version II dated 20 August 2022 that was provided have been read carefully by me / explained in detail to me, in a language that I comprehend, and I have fully understood the contents. I confirm that I have had the opportunity to ask questions.

मुझे इस अध्ययन की प्रकृति एवं उद्देश्य और इसके संभावित जोखिमों / लाभों तथा अध्ययन की अनुमानित अवधि एवं अन्य प्रासंगिक जानकारी के बारे में विस्तारपूर्वक समझा दिया गया है। मुझे पता है कि इस अध्ययन में मेरी भागीदारी स्वैच्छिक है तथा मैं इस अध्ययन से किसी भी समय बिना कोई कारण बताए, अपना नाम वापस लेने के लिए स्वतंत्र हूं और नाम वापस लेने पर मेरी चिकित्सा देखभाल या कानूनी अधिकारों पर कोई प्रभाव नहीं पड़ेगा। The nature and purpose of the study and its potential risks/benefits and expected duration of the study, and other relevant details of the study have been explained to me in detail. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal right being affected.

मैं समझता/समझती हूं कि इस अनुसंधान में मेरी भागीदारी से मेरे बारे में एकत्र की गई जानकारी और मेरे चिकित्सीय दस्तावेजों के किसी भी भाग को एम्स के जिम्मेदार व्यक्तियों द्वारा ही देखा जाएगा। मैं इन व्यक्तियों को मेरे रिकॉर्ड प्राप्त करने की अनुमति प्रदान करता/ करती हूँ। I understand that the information collected about me from my participation in this research and sections of any of my medical notes may be looked at by responsible individuals from AIIMS. I give permission for this individuals to have access to my records.

यदि प्रतिभागी बच्चा है तो उसकी मौखिक या लिखित सहमति प्राप्त की गई है। If participants is child, his/her verbal of written assent has been obtained.

मैं उक्त अध्ययन में भाग लेने के लिए सहमत हूं/I agree to take part in the above study.

_____
(प्रतिभागी के हस्ताक्षर / बांए अंगूठे का निशान) (Signature/Left Thumb Impression)

दिनांक/Date……स्थान/Place …….....

प्रतिभागी का नाम/Name of the participant…….....
पिता/पति/पत्नी का नाम /Son/Daughter/Spouse of…….
डाक का पूरा पता /Complete Postal Address ……..

अगर अशिक्षित हों / If illiterate.

सूचना पत्र को प्रतिभागी को पढ़ा और समझाया गया है और प्रश्न पूछने का अवसर दिया गया है। मैं पुष्टि करता हूं कि व्यक्ति ने स्वतंत्र रूप से अपनी सहमति दी है ।
The information sheet has been read and explained to the participant and given the opportunity to ask questions. I confirm that the individual has given consent freely.

कानूनी रूप से स्वीकार्य प्रतिनिधि या निष्पक्ष गवाह के हस्ताक्षर
Signature of Legally acceptable representative or impartial witness.
दिनांक/Date
एलएआर या निष्पक्ष गवाह का नाम / Name of LAR or impartial witness .
पता / Address :-

प्रमाणित किया जाता है कि उक्त सहमति मेरी उपस्थिति में प्राप्त की गई ।
This is to certify that the above consent has been obtained in my presence.

_____
छात्र शोधकर्ता के हस्ताक्षर दिनांक…….
स्थान……
Signature of the student Investigator Date …… Place
……

Age	Sex	Age at diagnosis	Symptoms at diagnosis	Height	Weight	BMI	Xray report	AFB /CBNAAT report	Rifampicin sensitivity	History of contact	Disseminated TB	Age of starting treatment	Duration of treatment	Duration till treatment completion	Oxygen requirement	HB	TLC	DLC	PLT	structure	MPI	TR Gradient	Systolic PAP(TR+10)	Peak PR Gradient	Mean PAP(PR+10)	PAA	PH	EF	e/E'
15	2	15	cough fever and cough	143	32	22	consolidation	1	1	1	2	2	15	6	5	2	12	7800	60/30	3.4	1	0.4	28	38	12	22	110	1	70	6
5	1	5	sputum with cough	116	18	13	Rlight upper lobe patch	1	1	1	2	2	5	9	8	2	10	###	46/55	4.1	1	0.3	21	31	8	18	143	0	65	6
15	1	14	cough and chest pain	148	30	14	left lobe bronchiectasis	1	1	1	2	2	14	6	10	2	13	9230	76/9	1.9	1	0.4	40	50	18	28	130	1	61	6
13	1	12	pain and cough fever and chest pain	151	38	17	consolidation and pleural effusion	1	1	1	2	1	12	6	6	2	12	8930	42/43	2.2	1	0.4	12	22	6	16	137	0	74	8
10	2	9	cough fever and	122	23	16	miliary pattern bilateral	1	1	1	2	1	9	12	3	1	11	9220	80/9	3.8	1	0.4	35	45	22	32	120	1	66	7
14	1	14	cough fever and cough pain abdomen	163	33	12	infiltrates right perihilar	1	1	1	1	2	14	6	7	2	13	6500	56/31	2.9	1	0.3	24	34	14	24	130	0	68	7
4	1	4		107	15	13	infiltrates upper lobe collapse left lower lobe bronchiectasis	1	1	1	2	2	4	6	10	2	13	3440	33/56	2.3	1	0.3	20	30	14	24	126	0	72	7
16	1	16	cough fever weight loss	166	48	18	Fibrocavitatory lesions in right lung	1	1	1	2	2	16	6	1	2	13	5600	47/40	3.5	1	0.5	35	45	14	24	120	1	63	8
18	2	18	cough Cough chest pain	154	40	17	left upper lobe fibrosis	1	1	1	2	2	17	10	4	2	8.2	###	89/4	2.6	1	0.6	44	54	32	42	108	1	69	7
15	2	15	fever cough weight loss	150	33	15	Fibrocavitatory lesions in right lung	1	1	1	2	2	15	6	11	2	13	7170	65/23	2.4	1	0.5	20	30	12	22	141	0	70	7
16	2	16	cough weight loss	150	35	15	Bilateral perihilar	1	1	1	1	2	16	6	9	1	9	###	34/59	3.5	1	0.5	42	52	30	40	110	2	62	6
13	2	13	cough fever cough chest pain cough weakness respiratory distress	140	30	15	infiltrate destroyed left lower lobe collapse with fibrosis	1	1	1	2	2	13	6	6	2	6.1	###	82/8.6	1.6	1	0.4	26	36	12	22	130	0	64	7
17	1	17		152	45	20		1	1	1	2	2	17	6	3	2	15	5120	38/50	2.5	1	0.5	22	32	6	16	140	0	67	7
12	1	11		150	47	21		1	1	1	2	1	11	6	12	1	9.4	###	80/1	6.8	1	0.5	12	22	5	15	102	1	65	6
15	1	15		163	60	23	normal	1	1	1	2	2	15	6	8	2	11	7780	83/10	0.9	1	0.4	14	24	6	16	139	0	69	8
14	2	13	fever and cough fever and cough fever and cough	137	31	17	right lung collapse left destroyed lung	1	1	1	2	1	13	12	2	1	12	7810	83/10	4.1	1	0.5	14	24	8	18	105	1	65	6
15	2	14		143	31	16		1	1	1	2	2	14	6	11	1	12	###	70/17	5	1	0.5	38	48	22	32	88	1	67	6
2	1	2		74	7	13	Normal left side pleural thickening	1	1	1	2	2	2	6	12	2	9	###	60/32.4	6.2	1	0.4	23	33	12	22	127	0	68	7
17	1	16		150	33	15		1	1	1	2	1	14	6	12	2	11	###	81/13	6.5	1	0.5	28	38	19	29	121	0	62	8

			cough and				left side pleural																					
17	1	16	pain fever cough shortness of	150	33	14.7	thickening	1	1	1	2	1	14	6	12	2	11.4	13940	81/13	6.52	1	0.5	28	38	19	29	131	0	62	8
8	2	8	breath cough	130	20.5	12.1	normal	1	1	1	2	1	2	8	6	1	7.9	19250	86/10	5.97	1	0.43	16	26	5	15	106	1	63	8
14	1	14	fever fever cough weight loss	148	35	16	normal	1	1	1	2	2	13	6	12	2	13	7900	34/43	3.2	1	0.46	12	22	6	16	147	0	70	7
12	1	11	chest pain fever cough weight loss	24.8	145	11.8	rt lung bronchiectasis	1	1	1	2	2	11	6	12	2	8.4	16720	67/18	5.6	1	0.37	24	34	12	22	121	0	63	6
13	2	13	pain couigh	125	30.4	19.5	bronchiectasis	1	1	1	2	2	13	6	11	2	8.7	7920	73/20	4.73	1	0.54	24	34	7	17	116	1	65	7
17	1	17	fever	165	49	18	normal	1	1	1	2	2	17	6	11	2	16	5760	53/37	2.71	1	0.48	12	22	6	16	144	0	66	
15	2	15	fever	148	34	15.5	Normal	1	1	1	2	2	15	7	3	2	10	8340	40/49	3.2	1	0.3	12	22	8	18	129	0	72	6
11	2	11	cough	138	27.5	15.7	mild right pleural thickening	1	1	1	2	2	11	6	9	2	12.8	10980	35/49	3.87	1	0.36	28	38	9	18	106	1	62	6
18	1	17	fever cough with	172	65	22.5	Normal	1	1	1	2	2	17	6	11	2	14	6500	66/23	4.5	1	0.3	12	22	6	16	142	0	67	6
17	1	16	sputum cough fever	170	56	19.4	Normal	1	1	1	2	2	16	6	12	2	10	4260	53/25	2.5	1	0.4	12	22	8	18	129	0	66	7
14	1	14	hemoptysis fever	150	35	15.6	left lower lobe bronchiectasis	1	1	1	2	2	14	6	3	2	11.4	9100	65/21	5.35	1	0.5	42	52	32	42	90	2	65	7
17	1	17	cough	171	56	19.3	Normal	1	1	1	2	2	16	9	9	2	13.4	11270	73/13	3	1	0.5	12	22	5	15	132	0	62	7
16	2	15	Fever cough generalised weakness fever	143	30.6	15.6	bil bronchiectatic changes	1	1	1	1	2	15	6	12	2	8.2	7100	74/21	3.49	1	0.45	8	18	5	15	110	1	68	8
17	2	16	cough shortness of breath cough	150	36	16	pleural thickening	1	1	1	1	2	16	9	6	1	10.8	7040	58/23	2.81	1	0.32	27	37	14	24	109	1	70	8
15	1	15	weight loss fever	162	56	21.9	Normal	1	1	1	2	2	15	6	4	2	12.6	8760	52/40	3.88	1	0.4	12	22	6	16	136	0	64	7
12	2	12	cough fever	134	36	20	Normal	2	1	2	2	2	12	6	7	2	12.8	3390	28/49	2.91	1	0.44	12	22	5	15	118	1	67	7
17	2	16	vomitin fever cough	155	39.6	16.5	pleural thickening	1	1	1	2	2	16	6	8	2	9	10800	27/73	9	1	0.33	8	18	4	14	120	0	65	7

3	1	3	Fever cough cough fever	86	9.9	13.3	pleural thickening RUL	1		1	2	2	3	6	12	1	11	#####	65\2 6	8.89	1	0.3	29	12	22	110	0	66	6
15	2	15	hemoptysis	148	29.2	13.3	pleural thickening	1	1	1	2	2	15	6	12	2	12.5	16800	79\8 .5	1.23	1	0.4	14	6	16	106	1	67	6
14	2	14	fever	149	30.2	15.5	bronchiectasis right lower lobe	2	2	2	2	2	14	6	12	2	10.8	10380	81\16 .7	4.2	1	0.45	32	16	26	110	1	68	7
18	1	16	cough	167	54	19.4	Normal	1	1	1	2	2	16	6	12	2	13	8900	69\2 1	3.1	1	0.3	14	6	16	131	0	64	8
12	2	11	fever cough weight loss fever	157	28.4	12.1	Normal	1	1	1	2	2	11	6	12	2	10	14148	85\1 0	4.98	1	0.36	23	6	16	148	0	65	6
17	1	17	cough	150	40	17.7	Normal	1	1	1	2	2	17	6	11	2	11	8700	46\3 6	2.4	1	0.3	20	6	16	146	0	71	8
15	1	15	cough	164	53	19.7	right lower lobe	1	1	1	2	2	15	6	12	2	8.2	7140	57\2 9	1.52	1	0.4	24	8	18	160	0	67	7
16	2	16	fever cough chest pain	158	31.9	14.1	Cavitatory changes in right middle and left upper	1	1	1	1	1	16	6	6	2	10	14180	85\1 0	4.97	1	0.37	10	4	14	180	0	74	6
16	2	16	fever cough	140	35	17.8	Left lower lobe infiltrates	1	1	1	1	1	16	6	7	2	8.9	13700	78\2 0	2.07	1	0.32	10	4	14	113	1	70	6
14	1	14	fever cough	171	52	17.8	pleural thickening	1	1	1	2	2	14	6	5	2	14	13740	74\1 6	4.65	1	0.3	10	4	14	140	0	64	6
15	2	15	fever cough vomitin	159	41	16.2	right pleural thickening	1	1	1	1	2	15	6	9	1	12	#####	89\5	7.13	1	0.46	20	4	14	99	1	63	8
5	1	4	cough fever chest pain	108	20	17.1	Right perihilar infiltrates	1	1	1	2	2	4	6	12	2	12.8	6580	56\3 6	4.38	1	0.4	28	10	20	126	0	66	8
15	2	15	shortness of breath fever	152	35.5	15.2	right lung fibrocavitatory lesion	1	1	1	2	2	15	6	3	1	7.8	8000	49\3 1	4.6	1	0.36	28	8	18	130	0	65	7
6	1	6	cough seizure	110	13	10.2	normal	1	1	1	2	1	6	9	3	1	9.6	9340	79.9 /12.3	5.73	1	0.31	10	4	14	120	0	68	6